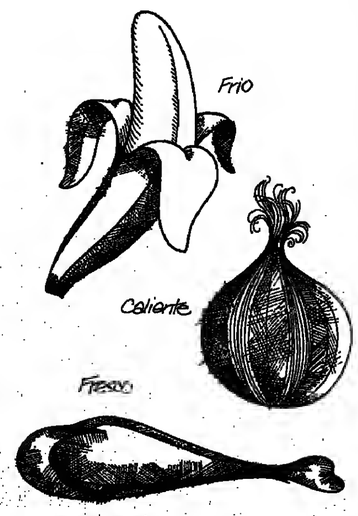
G.I. FORUM

A CURRENT REVIEW OF INVESTIGATIONS IN GASTROENTEROLOGY

Duodenal ulcer treatment and the "hot-cold" theory

A recent ethnographic study of a group of Spanish-speaking residents in New York City revealed an ancient "hot-cold" theory of disease not only still prevalent, but also compatible with some aspects of current ulcer management.[1]



The theory stems from the classic Greek humoral system of disease which was transferred to the New World by the Spanish and Portuguese in the 16th and 17th centuries. In the variant studied in New York, diseases and bodily conditions are classified as either "hot" (*caliente*) or "cold" (*frio*) and foods and medicines as "hot," "cold" or "cool" (*fresco*), irrespective of their actual temperatures. According to the theory, a "hot" condition should be treated with "cold" foods and medicines, and vice versa.[1]

Sometimes this presents a problem in modern medical management. For example, pregnant women often refuse "hot" iron supplements or vitamins in order to prevent their babies from being born with a rash, a "hot" condition. But in ulcer—another "hot" condition—the bland diet, still so frequently prescribed today, prohibits most of the foods considered "hot" within the folk system, including spices and coffee.[1]

Milk, chicken breast—and horseradish?

However, the bland diet itself now tends to be considered in many quarters almost akin to folk medicine. One investigator notes that since the time of the 19th century French pathologist Jean Cruveilhier, the bland diet has been synonymous with the "white" diet—milk, chicken breast, cottage cheese. But what about white horseradish? he wonders. His point—much of dietotherapy by analogy may be ludicrous.[2]

Milk, antacid and hospitalization

Further thrust to this argument was given by controlled studies alternating an unrestricted diet with a standard bland diet in patients dingnosed as having active duodenal ulcer. One such study, in Iowa, showed no significant difference in healing rates, symptoms or recurrences between patients given a bland diet and those given a standard one.[3]

A British observer[4] states that while these results suggest diet has no effect on the remission of duodenal ulcer, they do not constitute absolute proof. To begin with, all of the patients were given regular and frequent doses of milk and antacids. But most important of all, they were hospitalized for purposes of the study. And hospitalization alone is known to bring relief to the ulcer patient.[4]

References: 1. Harwood, A.: *J.A.M.A., 216*:1153, 1971. 2. Ingelfinger, F.J.: "Let the Ulcer Patient Enjoy His Food," in Ingelfinger, F.J.; Relman, A.S., and Finland, M. (eds.): *Controversy in Internal Medicine*, Philadelphia, W. B. Saunders Co., 1966, p. 173. 3. Buchman, E., et al.: *Gastroenterology, 56*:1016, 1969. 4. Diet and Duodenal Ulcer, *Brit. Med. J., 3*:727, 1969.

Librax®—for excessive anxiety and related G.I. symptoms

Excessive anxiety can be a major triggering stimulus, inducing gastrointestinal hypersecretion and hypermotility and frequently leading to ulcer exacerbation in a susceptible individual. For many duodenal ulcer patients hospitalization may be unwarranted, long vacations impractical—but they still need respite from hypermotility and hypersecretion which produce spasm and associated pain. In many cases, adjunctive Librax can help. Only Librax offers in a single capsule the well-known antianxiety action of Librium® (chlordiazepoxide HCl) and the antisecretory/antispasmodic action of Quarzan® (clidinium Br).

The logic of dual-action therapy

The action of Librium usually helps reduce excessive anxiety which may accentuate the somatic symptomatology of duodenal ulcer. At the same time, the action of Quarzan, a dependable anticholinergic, helps reduce gastric hypersecretion and hypermotility—thereby helping to relieve spasm and associated pain.

While the evidence is inconclusive regarding the precise role dietotherapy may play in gastroenterologic medicine, the value of adjunctive Librax in the total medical management of the peptic duodenal ulcer patient has been clearly demonstrated.

Up to 8 capsules daily in divided doses

For optimum response, dosage may be adjusted to your patients' requirements, within the range of 1 or 2 capsules, 3 or 4 times daily.

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Symptomatic relief of hypersecretion, hypermotility and anxiety and tension states associated with organic or functional gastrointestinal disorders; and as adjunctive therapy in the management of peptic ulcer, gastritis, duodenitis, irritable bowel syndrome, spastic colitis, and mild ulcerative colitis.

Contraindications: Patients with glaucoma; prostatic hypertrophy and benign bladder neck obstruction; known hypersensitivity to chlordiazepoxide hydrochloride and/or clidinium bromide.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. As with all CNS-acting drugs, caution patients against hazardous occupations requiring complete mental alertness (e.g., operating machinery, driving). Though physical and psychological dependence have rarely been reported on recommended doses, use caution in administering Librium (chlordiazepoxide hydrochloride) to known addiction-prone individuals or those who might increase dosage; withdrawal symptoms (including convulsions), following discontinuation of the drug and similar to those seen with barbiturates, have been reported. Use of any drug in pregnancy, lactation, or in women of childbearing age requires that its potential benefits be weighed against its possible hazards. As with all anticholinergic drugs, an inhibiting effect on lactation may occur.

Precautions: In elderly and debilitated, limit dosage to smallest effective amount to preclude development of ataxia, oversedation or confusion (not more than two capsules per day initially; increase gradually as needed and tolerated). Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (e.g., excitement, stimulation and acute rage) have been reported in psychiatric patients. Employ usual precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants; cause relationship has not been established clinically.

Adverse Reactions: No side effects or manifestations not seen with either compound alone have been reported with Librax. When chlordiazepoxide hydrochloride is used alone, drowsiness, ataxia and confusion may occur, especially in the elderly and debilitated. These are reversible in most instances by proper dosage adjustment, but are also occasionally observed at the lower dosage ranges. In a few instances syncope has been reported. Also encountered are isolated instances of skin eruptions, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased and decreased libido—all infrequent and generally controlled with dosage reduction; changes in EEG patterns (low-voltage fast activity) may appear during and after treatment; blood dyscrasias (including agranulocytosis), jaundice and hepatic dysfunction have been reported occasionally with chlordiazepoxide hydrochloride, making periodic blood counts and liver function tests advisable during protracted therapy. Adverse effects reported with Librax are typical of anticholinergic agents, *i.e.*, dryness of mouth, blurring of vision, urinary hesitancy and constipation. Constipation has occurred most often when Librax therapy is combined with other spasmolytics and/or low residue diets.

helps relieve anxiety-linked symptoms in duodenal ulcer

adjunctive

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Medical Tribune

and Medical News

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New FDA Labeling

Way Is Paved To Better MD Food Advice

Medical Tribune Report

WASHINGTON—The Food and Drug Administration's new voluntary food-labeling policy has opened the way "for more rational nutritional advice from the physician to his patient," according to nutrition experts.

They predicted that the new regulations, which will become effective over the next two years, will increase both the opportunities and the pressures for doctors to provide nutritional guidance.

DR. MAYER

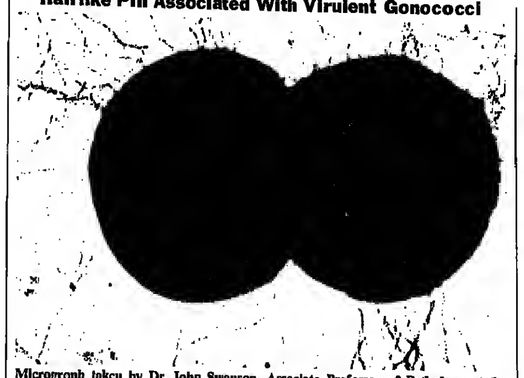
"Up to now, we've had a more or less 'hands off' policy by most physicians with regard to nutrition because, without exact knowledge of what was in processed foods, recommendation of specific foods and a particular diet was difficult," MEDICAL TRIBUNE was told by Jean Mayer, Ph.D., Professor of Nutrition, Harvard School of Public Health, and a long-time advocate of food-labeling changes. "As a result, not enough attention was given to nutritional considerations."

Doris Calloway, Ph.D., Professor of Nutrition at the University of California at Berkeley, said that "the new relabeling procedure will not relieve the physician of any responsibility concerning his patient's nutritional needs."

She added that the relabeling may prove

Continued on page 12

Hairlike Pili Associated With Virulent Gonococci



Micrograph taken by Dr. John Swanson, Associate Professor of Pathology at the University of Utah, shows pili present on cell walls of Neisseria gonorrhoeae. Dr. Swanson has found pili present on disease-producing gonococci but absent from nonvirulent strains. With other researchers he has developed a promising serologic screening test for gonorrhea, in which antibodies created in response to pili are detected. Other investigators have linked pili to possible R-factor transfer.

2 More Doctor Units Sign Up As Unionizing Trend Grows

Medical Tribune Report

NEW YORK—In what may be the harbinger of a national trend, physicians in two hospitals, one on the West Coast and the other on the East, have signed up with the A.F.L.-C.I.O. to form collective bargaining organizations.

They are the second and third groups of physicians recently reported to have taken such steps.

The first was composed of physicians in private practice who were members of the utilization review committee of Valley Hospital, Las Vegas. In a trail-blazing step last October, they obtained a collective bargaining contract signed by Nevada Physicians Local 676 and the hospital (MEDICAL TRIBUNE, October 18, 1972). The union, part of the Service Employees International of the A.F.L.-C.I.O. claimed to represent 62 of the 280 physicians in the Las Vegas area.

The two latest M.D. groups to organize comprised house staff members at the Contra Costa County Hospital, Martinez, Calif., and the municipally operated Jersey City (N.J.) Medical Center.

The action taken by the Contra Costa physicians followed upon the merger by

Continued on page 27

Test Employing Cold Stimulus Shows Sclerosis

Medical Tribune Report

SAN JUAN, P.R.—Intensive computerized testing has confirmed the hypothesis that the cold-pressor test, developed in the 1930s for indicating prehypertensive states and later virtually abandoned, is effective as a screening test for arteriosclerosis.

Dr. Ignatios J. Voudoukis, chief of the hypertension section of the Hutzel Hospital Unit, Wayne State University School of Medicine, said here that "excessive acute blood pressure elevations (systolic and pulse pressure) precipitated by a cold stimulus should be considered as an indication of clinically significant atherosclerotic vascular disease rather than hypertension."

DR. VOUDOUKIS

Speaking at the 19th Annual Meeting of the American College of Angiology, Dr. Voudoukis suggested that "any individual with exaggerated cold-pressor response should be further investigated for clinically significant vascular sclerosis."

Cold-pressor response was determined in 641 consecutive ambulatory patients of a predominantly hypertensive population seen in a solo private practice. They were divided into four groups—83 patients free of hypertension and arteriosclerosis, 66 with arteriosclerosis, 93 with hypertension, and 399 who had hypertension with superimposed arteriosclerosis.

All patients were given base-line blood pressure and cold-pressor tests. Blood pressure was taken at five-minute intervals for 30 minutes. The lowest blood pressure, "usually obtained at about 20 minutes from the initiation of the procedure," was designated the base-line blood pressure.

Continued on page 27

Jackson Is Stonewalled

Amphetamine Regimen Calms Vicious Dog

Medical Tribune Report

WASHINGTON—The case history of a hyperkinetic dog whose extreme violence and viciousness disappeared within an hour after dextroamphetamine therapy and has not recurred was outlined here by an Ohio investigator during the annual meeting of the American Association for the Advancement of Science.

The experiment suggests that certain drugs may eliminate "some types of violent behavior that cannot be controlled by any form of psychosocial therapy," said Samuel A. Corson, Ph.D., Professor of Psychiatry at Ohio State University College of Medicine.

Dr. Corson described the dog, Jackson, as spontaneously and aggressively vicious. A beagle-cocker spaniel hybrid, he responded to any approach with snapping, snarling, growling—or, if possible, biting—and in the course of a notorious career in the laboratory had attacked other dogs, bitten experienced and gentle handlers, and ruined considerable equipment when pavlovian conditioning was attempted.

Tranquilizers failed to help, and since the 18-month-old dog also exhibited hyperkinesis the decision was made to try amphetamine, embedded for safety's sake in a meatball. The dosage approximated that used with hyperkinetic children.

Vicious barking and snarling disap-

Continued on page 12

Hyperkinetic dog before, l., and after D-amphetamine therapy, with Dr. Corson.

Significance of K Drain In Diuresis Doubted

Medical Tribune World Service

ROME—The significance of serum potassium deficiency in patients undergoing diuretic therapy, especially for hypertension and cardiac edema, was disputed here by cardiologists.

Drs. Pierre Delwaide and George Rorive, of University Hospital, Liège, Belgium, reported that isotope studies of potassium[40] failed to show a correlation between serum K and total body K. In patients treated with diuretics, total body K was normal despite a low serum K and alkalosis, they said.

A British expert, Dr. Alastair Breckenridge, of Hammersmith Hospital, London, contended that KCl supplements were almost entirely excreted in urine and that signs of K deficiency do not appear until about 30 per cent of body K has been lost.

"Are we trying to treat the patient or his serum K level?" he asked.

Vascular Operation Tried Successfully In Sexual Impotence

Medical Tribune World Service

PRAGUE—Microvasculsr surgery to trsnsplant n saphenous vein segment has been used successfully here in tho treatment of selected cases of sexual impotence at the Institute of Clinical and Experimental Medicine.

The first case was that of an automobile accident victim with pelvic fracture and extensive hematomata and internal bleeding in the pelvic and genital region, which required tying off of the internsl iliac branches.

The patient was rendered impotent, and Dr. Vaslav Michal was asked to perform aortographic studies. These abowed poor circulation to tbe eotire pelvic region. Dr. Michal conducted e literature study, with meager results, he related: combinations of atheromatous plaques and poor circulation in the lower extremities with impotence were known, but surgical attempts at correction were few and of doubtful value.

Endarterectomy Considared

Several previous reports were conceroed with iliac endnrterectomy to improve circulation to the penis, but while 30 per cent of the patients showeil some improvement lo erection, another 30 per cent showed no change, and even in the improved cases, ejaculation had usually disappeared completely.

Dr. Micbal believes tbat the latter complication camc about because the surgery was intrapelvic and required interruption of the pelvic autonomic nerve plexuses involved in the ejaculation reflex. In his own first case, further intrapelvic surgary was out of the question, he said, since previous surgery had left the terrain unrecognizoble, aad so he began to work out an extrapelvic approach. This called for surgery carried out under a dissecting microscope with specal instruments—a technique in which he had been trained during a year'a stny with Prof. Julius H. Jncobson II at the Mount Sinsi Hospital, New York.

The first approuch tried, which worked completely and immediately, Dr. Michal reported, was to use a deep snplienous vein segment as a graft, attoching one end to the pudendal artery exposed from the perineum and otber end to the mediol aide of the femoral artery, both junctlons end-to-side, with the graft being led subcutaneously along the scrotum and then hy tunneling into the femorul triangle. The microsurgery wns necessitnted by the smnll size of the gmft and the pudendal nrtery.

Sexual competence returned within n few dnys of surgery.

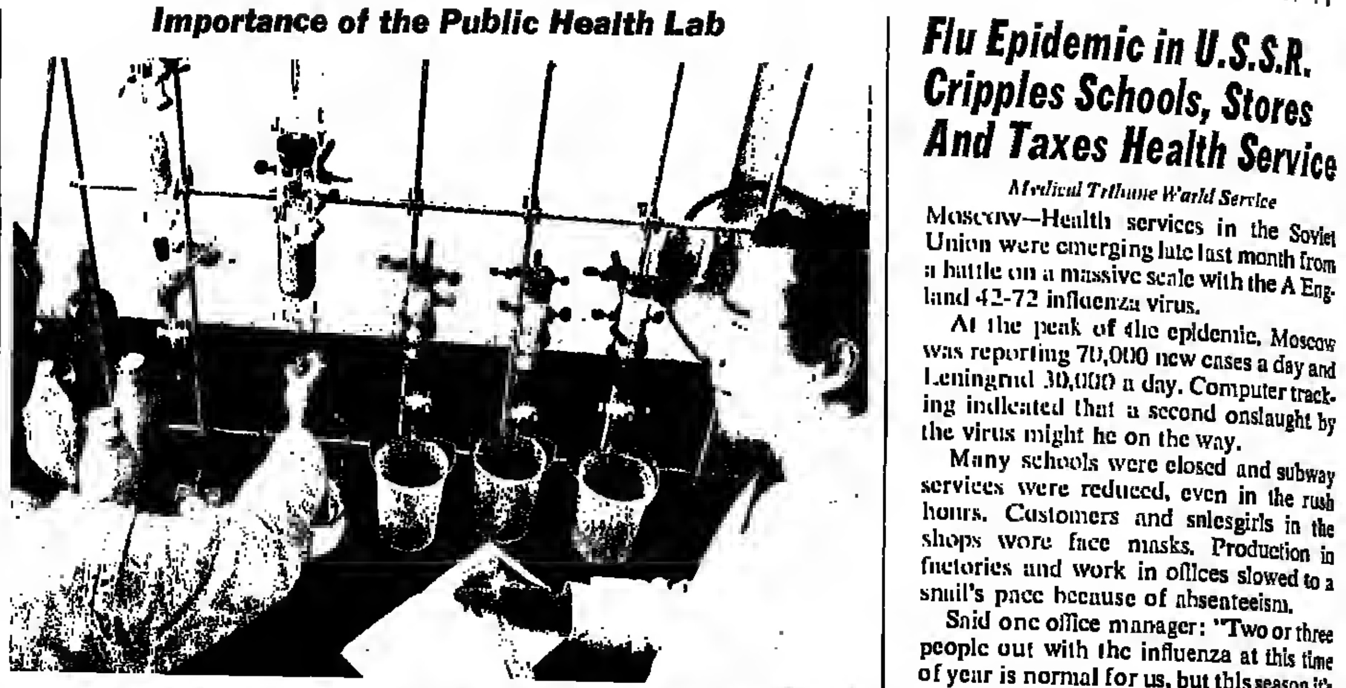
The oparation itself, Dr. Michnl commentad, is simplo, rapld, and rolntively untmumatic—two smnll inoisions ond only subcutaneoua dissection. He performed the operation eight times on cadnvers before the first clinlcnl ottempt.

After the first successful experience, he turned his attention to the for more common case of impotence caused hy atheromatous plaques, and developed an nortographic technique in order to nnalyze the vascular situation.

One of his mnin research interests ut present is the development of n reliable dingnostic test for a vascular hasis of impotence. His approach is to measure hlood flow in the penis with either thermistors or impedance plethysmography. His problem is how to induce erection by constunt and relinble technique, and he is trying to use such peptide drugs ns vnsopressin.

■

Importance of the Public Health Lab



WHO Photo

The public health leboratory is an essentiel tool of every public health servlce in the world. The laboratory is needed to defina the magnitude of certoln disease problems, to determine the control strategy, end to help in appraising the degree of success in disease control. Above, at Chilean public health lab., milk is tested for strontium⁹⁰.

Flu Epidemic in U.S.S.R. Cripples Schools, Stores And Taxes Health Service

Medical Tribune World Service

MOSCOW—Health services in the Soviet Union were emerging late last month from a battle on a massive scale with the A England 42-72 influenza virus.

At the peak of the epidemic, Moscow was reporting 70,000 new cases a day and Leningrad 30,000 a day. Computer tracking indicated that a second onslaught by the virus might he on the way.

Many schools were closed and subway services were reduced, even in the rush hours. Customers and salesgirls in the shops wore face masks. Production in factories and work in offices slowed to a snail's pace because of absenteeism.

Said one office manager: "Two or three people out with the influenza at this time of year is normal for us, but this season it's 15 or 20 out at once. A lot of the work has just come to a standstill."

When Leningrad was alerted the flu virus was approaching, children were on year-end vacation, so the vacation was prolonged while certain day nurseries and crèches began working round the clock.

Musoum Queuas Disappeared

The always familior long queues of Moscow schoolchildren going to visit museums disappeared during the epidemic. For those schools that were open, excursions were banned.

In cinemas in Moscow, Leningrad, and other main cities, long intermissions were introduced between showings to allow disinfection of the premises.

An "Influenza task force," headed by Dr. Piotr Bourgasov, Deputy Minister of Health, with a flu warning system linking 122 cities, was established. Its object was to advise the population on precautions to be taken and to organize and direct all health services mobilized for the battle.

For the past three years the number of cases has not gone above what Dr. Bourgasov calls a "normal level" for influenza, but this year much of the population had lost the two or three years' immunity carried from the last attack of the virus.

"We haven't beaten the virus," Dr. Bourgasov commented, "but with the precautions we took we have been able to limit the spread of infection and to prevent in many cases the complications that increase mortality."

■

Motorbike Mishaps Cited

Medical Tribune World Service

THE HAGUE—Young persons between the ages of 15 and 19 havo a higher rate of hospitalization and mortality from accidents than any other nge group in the Netherlands, according to n report by the Dutch Medical Registration Foundation.

Traffic occidents account for most of tho cases, and most of the victims are riders of light motorcycles.

■

Australian MD Group Is Opposed To New Government Health Plan

Medical Tribune World Service

CANBERRA — Health care plans by Australia's newly elected Labor Government face stiff opposition from the Australian Medical Association.

Timing for the introduction of Labor's proposed single-fund insurance plan—to be financed by a tax surcharge—will depend on the cooperation of the doctors, Prime Minister Edward Gough Whitlam has declared.

But the medical association has already announced it will oppose any move by the Oovernment to abandon tho present voluntary health insurance scheme or to turn physicians into salaried civil servants.

■ ■ ■

Australians Claim Success in Program To Return Women Doctors to Medicine

Medical Tribune World Service

SYDNEY, AUSTRALIA—A plan to help women doctors rotum to tbo professioo if they have been away from medicine for some tima is working successfully here.

The three-month retraining course, instituted last year, is conducted by the Mater Misericordiae Hospital, North Sydney, under the guidance of the clinical superintendent, Dr. Geoffrey Dietbelm.

Five women have already completed the program. Most of them had been away from medicine as long as 10 years. All are housewives and mothers whose family involvements bad taken up most of their time since graduation.

Today, all are back in general practice.

The retraining course provides for a thorough reintroduction to geoeral practice aod includes training with new drugs and therapeutic methods and a general brush-up.

■

Half of Blind Are Indian

Medical Tribune World Service

NEW DELHI—Physicians here estimate that India's blind now number some 10,000,000 persons, half the world total. Most of them live in Uttar Pradesh.

The health minister of that state, Dharam Datta Valdya, told a conference of eye surgeons in Hatras that blindness caused by infectious diseases is on the decline, but that blindness caused by malnutrition is on the increase, particularly among children and expectant mothers.

Eradication of Smallpox By 1975 Is Foreseen

Medical Tribune World Service

GENEVA, SWITZERLAND — The World Health Organization predicted here that smallpox would be eradicated by 1975 if present programs are maintained. WHO's Executive Board reported that, although smallpox incidence last year increased to about 65,000 cases, that figure represented better reporting and diagnosis.

With the exception of Bangladesh, Pakistan, and India, where major outbreaks occurred, there were relatively few cases in the world.

NEWS INDEX

CLINICAL NEWS NOTE: *"Insofar as it is valid to extrapolate from animals to humans,... what hyperkinetic or violent children learn in school while medicated with amphetamine they would tend to retain later." (S. A. Corson, Ph.D., see page 1.)*

FEATURE INDEX

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Child Health Center Serves Chicagoans

The Woodlawn Child Health Center, located on Chicago's South Side, provides free comprehensive health services to children in the Woodlawn area who need primary health care aod preventive services. Above, Dr. Alberto Gedissman, one of four pediatricians supplied by the University of Chicago Pritzker School of Medicine, with patient. At right, Veronica Chandler works with the files of the Center's 16,000 registered patients.

Lab technician Beatrice Coin at work in the center's laboratory. According to Dr. John Madden, medical director, the presence of the center in the community has been a contributing factor to the improved general health around Woodlawn.

Rheumatoid Arthritis

Subgroup of Patients Responds to Histidine

Medical Tribune Report

PITTSBURGH—A study of histidine treatment in patients with rheumatoid arthritis suggests that a subgroup of patients with severe active disease of long duration may experience a modest degree of clinical improvement after having undergone this form of therapy.

This finding was reported at the interim scientific session of the American Rheumatism Association by Dr. Robert S. Pinals, of the State University of New York, Upstate Medical Center, Syracuse.

Low serum levels of histidine in patients witb rheumatoid arthritis have been reported by several investigators, Dr. Pinals noted, although a satisfactory explanation for the phenomenon has not been produced.

In the present investigation, performed at Upstate Medical Center and at Dartmouth-Hitchcock Medical Center, Hanover, N.H., 60 patients evenly matched for age and with definite rheumatoid arthritis were placed at random on identical capsules of 4.5 mg. L-histidine daily or placebo for 30 weeks.

Response to Treatment Compared

Evaluation of response to treatment revealed no significant differences between the two groups in grip strength, sedimentation rate, walking time, morning stiffness, or number of swollen and tender joints, Dr. Pinals reported.

Neither was there significant improvement in these parameters within each group, except in hematocrit in the histidine-treated patients and the grip strength in tha placebo group.

But when correlations were made betweeo patients' impressions to certain clinical characteristics at the beginning of the study and subsequent responses to treatment, several interesting findings appeared.

Patients with long duration of illness, seropositivity, greater walking impairment, and higher sedimentation rates improved significantly more often on L-histidine. Earlier and less severe cases had a better result on placebo.

Physician evaluations were found to yield a somewhat similar pattern of results.

Because of the small group of patients studied and the variation in histidine levels on different days, it was not possible to make significant clinical correlations, said Dr. Pinals, but there was a suggestion that lower serum levels of histidine were associated with superior therapeutic results.

Levels increased in the histidine group but not in the placebo group during the study.

"On the basis of this study, we must say that the therapeutic efficacy of histidine has not yet been established and that general use of this treatment cannot be recommended," said Dr. Pinals.

Co-workers were Drs. Edward D. Harris, Jr., and James Frizell, of Dartmouth Medical School and Dr. Donald A. Gerber, of the State University of New York, Downstate Medical Center, Brooklyn.

Imprinters to Help MDs Cut Misuse of Drugs

Medical Tribune Report

CINCINNATI—To help pharmacists in dispensing medication and to reduce prescription forgeries, the University of Cincinnati Medical Center will issue imprinters to physicians on the house staff. The imprinter is a stamp with the physician's name and indentification number.

It is also hoped that they will eliminate inconvenience experienced by patients when prescriptions cannot be filled because of illegible signatures.

This program to control hospital prescription blanks is the first in Ohio and may be unique in the nation, the medical center said.

The innovation was suggested by Robert Bundman, chief pharmacist at Holmes Hospital.

10% of NYers Screened Are Hypertensive

Medical Tribune Report

NEW YORK—Nearly 10 per cent of adult New Yorkers screened in the first year of a Health Services Administration hypertension control program were found to have high blood pressure, HSA administrator Gordon Chase announced.

He reported these results:

- Of 67,165 adults screened, 9.8 per cent had a diastolic pressure of 100 mg. Hg or over and were referred for treatment, and 2.9 per cent were considered borderline (95-99 for persons 35 years of age and older) and were advised to have another blood pressure measurement.
- Of 14,583 high school–age subjects screened, 3.5 per cent were found to have significantly elevated blood pressures (90 mm. Hg or over).

Mr. Chase commented: "I'm especially pleased that we have been able to get the program off the ground so fast. So far as I know, no other government in the country is doing anything like the massive testing we are doing.

"HSA's screening program already has been very useful in term of public education. We've helped to make more New Yorkers aware that high blood pressure is a serious health problem.

"Now that HSA's program has shown many New Yorkers that they have high blood pressure, we are concerned about what these people do with that information. We suspect that many do nothing more than make a mental note of it. The major thrust of HSA planning for hypertension control in 1973 will be to set up and evaluate pilot treatment programs for victims of high blood pressure."

A.C.S. and NCI Name First of Projects For Early Detection of Breast Cancer

Medical Tribune Report

NEW YORK—The first three of 20 planned demonstration projects for the detection of breast cancer in its early stages were announced by the American Cancer Society and the National Cancer Institute.

The selections were announced by Dr. Arthur James, president of the A.C.S., and Dr. Frank J. Rauscher, Jr., director of the NCI.

The three sites are: the Stella and Charles Guttman Breast Diagnostic Institute, New York; Emory University School of Medicine, in cooperation with the Georgia Baptist Hospital, Atlanta; and the University of Louisville School of Medicine.

At least 5,000 women, many from low-income families, will be screened annually at each facility. At the same time, various combinations of advanced diagnostic methods will be evaluated, and local physicians and allied health professionals will be trained in the various techniques.

ECTOPIC BEAT

"The low price includes round-trip jet transportation including meals and beverages; a double room with private balcony; American breakfasts every morning; five full-course dinners, including a Caribbean luau and a barbeque. . . ."

—*Bulletin* of the Beaver County (Pa.) Medical Society.

A Caribbean luau is a calypso hula, but what's a barbeque?

(Regular beat: Immateria Medica, page 35.)

Exposure to Cadmium May Pose Threat to Man

Medical Tribune Report

WEST LAFAYETTE, IND.—Exposure to cadmium may pose an environmental threat to man, a team of 16 Purdue University students reported to the National Science Foundation.

The team spent 11 weeks last summer investigating the levels of cadmium in the environment in a program called Student-Originated Studies, cosponsored by the National Science Foundation and Purdue's Institute for Environmental Health. The director of the Purdue project was John E. Christian, Ph.D., chairman of the Department of Bionucleonics.

Utilizing radioisotopes and radiation counters in one portion of the investigation, the students found that all species studied exhibited high retention of cadmium—up to 96 per cent nine weeks after exposure—after intravenous administration. Cats, rats, mice, sheep, rabbits, dogs, and goats also showed retention of more than 90 per cent in all instances after intraperitoneal administration.

The liver concentrated the major portion of the cadmium retained in the body, the kidney the next highest, followed by the pancreas and spleen.

Total Depositions Listed

"It was interesting to note the sum total deposition of cadmium in the liver and kidney of the larger species," the students said. "Adding together the percentages in the liver and kidney, a total deposition of 98.8 per cent in sheep, 98.6 in goats, and 98.15 in dogs was shown.

"This is excellent agreement and is typical of what might be expected in human subjects exposed to small amounts of cadmium each day. Although the dispersion of cadmium in food chains is poorly monitored, and concentrations in normal diets must necessarily be approximated, it is estimated that the daily oral human intake in industrial areas lies in the range of 200 and 400 micrograms."

Between 1 and 2 per cent of this amount is absorbed and reaches the bloodstream, the students continued. Taking the average daily dietary intake to be 100 micrograms of cadmium, then 1 to 2 micrograms enters the bloodstream and would be expected to be almost completely retained in the liver and kidney.

"Over the lifetime of the individual, amounts accumulated in these organs could result in impairment of health," they said. "This is particularly true when one considers that only 1.75 micrograms per day in the bloodstream appears to initiate subtle hypertension effects.

"The logical conclusion is that, since cadmium is an accumulative poison, being retained primarily in two vital organs of the body, current levels of intake already may be hazardous in some areas of the United States."

IN CONSULTATION

What's new and important in rheumatology?—I

The Consultant

DR. LEE E. BARTHOLOMEW

Professor of Rheumatology,
Head, Division of Rheumatology,
Albany Medical College, Union University, Albany, N. Y.

THE IMMUNOLOGY of connective-tissue diseases probably takes the forefront at the present time. Systemic lupus erythematosus, being the prototype of the immune complex diseases, is the subject of much interesting and exciting work. The fact that there are several antinuclear antibodies which have been described, and probably many more yet to come, provides considerable interest to the possibilities of subdividing these diseases in terms not only of prognosis but of different therapeutic approaches. Along this line, the description of the mixed connective-tissue disease syndrome by Dr. Gordon Sharp and others and its relationship to a specific antigen-antibody reaction, the antigen ENA (extractable nuclear antigen), and the presence of very-high-titered antibody to this antigen in patients with this syndrome, is one such example. This appears to be a variant of scleroderma—which, interestingly, responds to high doses of steroids.

Antibody directed against both native DNA and denatured or altered DNA, as seen in the fluorescent antibody method as either a "peripheral" or "shaggy" fluorescent pattern and in a number of the connective-tissue diseases, probably represents the immune complex responsible for lupus nephritis, particularly the native DNA-anti-DNA complex. The antibody directed against nucleoli appears to be specific for scleroderma. Other antigen-antibody reactions have been studied, such as the saline soluble antigen, which also causes a speckled pattern, and the nucleoprotein-antinucleoprotein pattern, responsible for the LE preparation, which gives a homogeneous pattern on fluorescent antibody methods.

It is also apparent that there are antibodies directed against cytoplasmic components in patients with lupus. The binding of RNA by the serum of patients with lupus indicates that anti-RNA and anti-RNA-protein antibodies are also present in this disease and may have their own significance.

It is apparent that we can revise some of our concepts. For example, young teenagers who present with what appears to be polyarthritis of the rheumatoid type may well represent the first manifestation of ankylosing spondylitis in childhood. Several reports have dealt with this condition, and it is important that children in teenage presenting with polyarthritis have their sacroiliac joints x-rayed to pick up early manifestations of ankylosing spondylitis. The therapeutic program is quite different for this condition. The outlook is perhaps more favorable than ever, and prevention of spinal deformities can be started early in the course of the disease.

An interesting iatrogenic disease is that of the arthritis associated with rubella vaccination. For years it has been known that certain epidemics of rubella were associated with a rheumatoidlike arthritis. This arthritis might last for several weeks or even several months after the acute manifestations of rubella subsided. Now that vaccination is being used almost routinely in younger age groups, a postvaccination arthritis is being seen, and it is important to know of the benign nature of this disease, that it responds well to salicylates in the usual doses, and that it is indeed not rheumatoid arthritis.

What is the status of gold therapy in the treatment of adult rheumatoid arthritis?

The basic conservative program of the treatment of rheumatoid arthritis in the adult consists of adequate salicylates; that is, blood levels between 15 and 25 mg. per 100 ml. two or three hours after taking their last dose of aspirin, adequate rest (both body rest and joint rest) for the acute phases of the disease. Simple measures, such as cock-up splints for the hands and wrists to be worn at night and during the day, are extremely useful during acute flares of synovitis involving those joints. The third basic conservative measure is that of physical therapy, which includes not only the use of heat, such as the Hubbard tank, paraffin to the hands and fingers, hot packs, Hydrocollator packs, etc., but also the cautious use of range-of-motion exercises to prevent deformities and muscle-strengthening exercises of individual muscle groups which have become atrophied.

This basic program is given for periods of two to four months. If at the end of that time there has not been adequate suppression of this disease in terms of decrease in morning stiffness, fewer joints showing active synovitis, increase in well-being and less general fatigue and malaise, and improvement in sedimentation rate and anemia, additional therapy is then indicated. I personally feel that the use of intramuscular gold salts is not only the most potent but the most effective of the anti-inflammatory agents used for rheumatoid arthritis. It is not without its hazards and toxicity, and for this reason great care should be taken in using the gold salts. This requires a cooperative patient, a patient who is willing to come in to see the physician regularly. Before each injection, complete blood counts, evaluation of platelets, complete urinalysis are performed, the patient is observed for skin rashes, oral mucous membrane lesions, and questioned concerning whether they are developing any pruritus.

Patients are usually given 5 to 10 mg. at the first injection, 25 at the second, and then 50 mg. weekly until approximately 1 Gm. of gold has been given. Usually, if response is to occur it begins somewhere between 500 and 1,000 mg., and if they respond well, a maintenance program is established for an indefinite period using 50 mg. intramuscularly every month. If signs of toxicity occur the drug is withheld, or if significant toxicity occurs the drug is stopped completely. Using this cautious approach, rarely do significant toxic reactions occur.

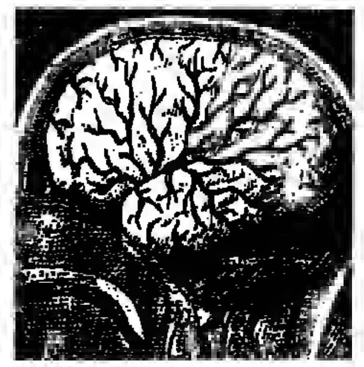
In general, one can expect that approximately 50-60 per cent of patients who can tolerate the drug will have improvement. Many of them will have a complete remission that may last for years.

Next week Dr. Bartholomew will discuss the immunologic aspects and treatment of systemic lupus erythematosus.

HERE Muscles and joints

Wherever it hurts, Empirin Compound with Codeine usually provides the symptomatic relief needed.

HERE Headache



In flu and associated respiratory infection, Empirin Compound with Codeine provides an antitussive bonus in addition to relief of pain and bodily discomfort.

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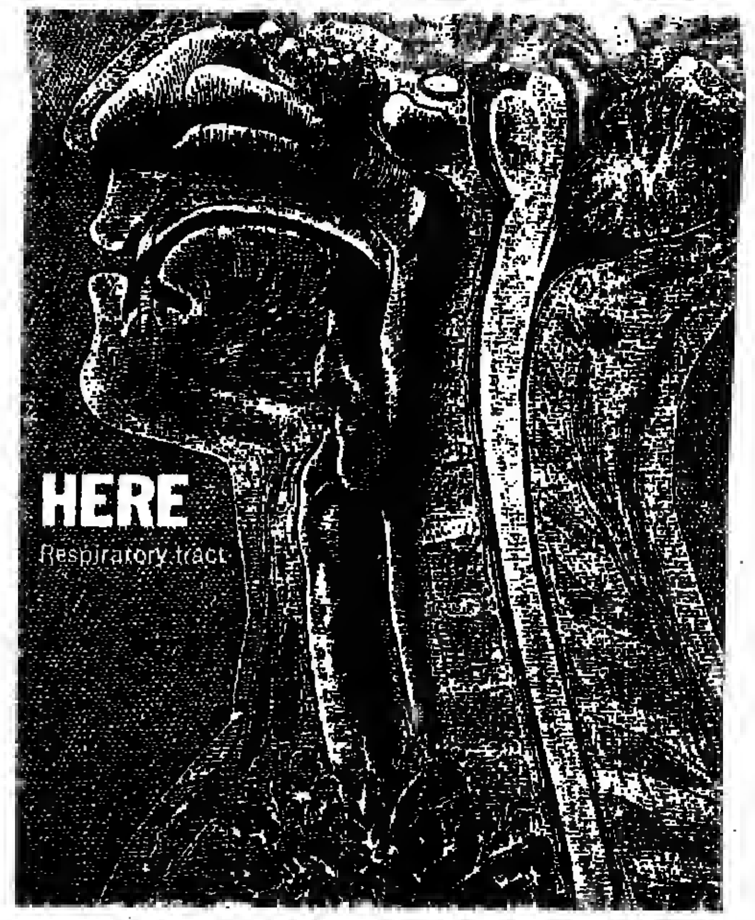

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Questions doctors are asking about Tranxene®
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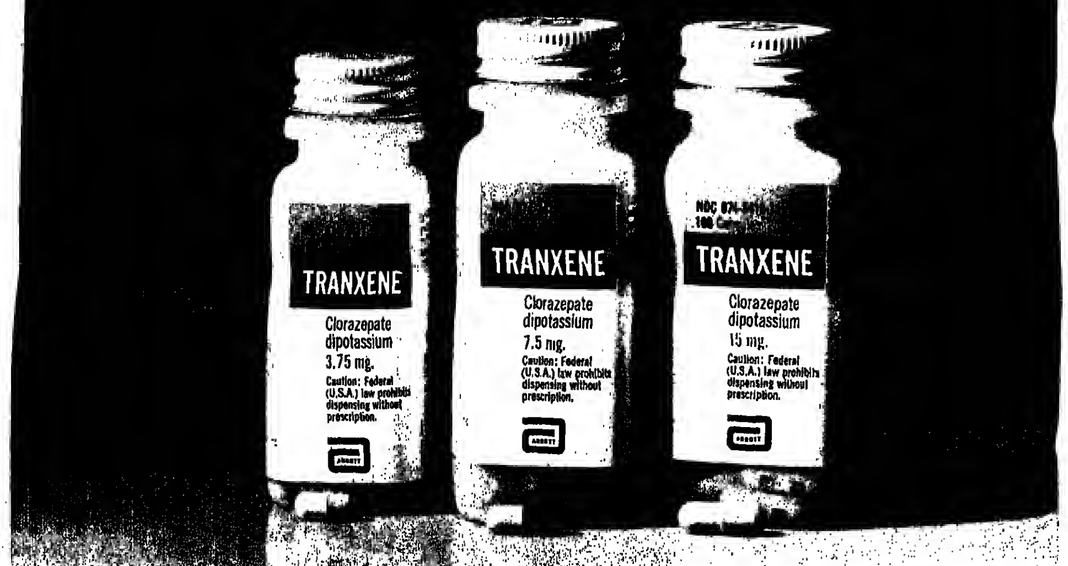


the new benzodiazepine from Abbott

About these questions, Doctor:

Since the introduction of our new anti-anxiety agent, Tranxene (clorazepate dipotassium), in early October, we have maintained an 8:00-to-5:00, private-line communication system with our field representatives for the purpose of gathering and answering questions being raised daily by physicians.

The questions presented here are among those most frequently discussed, and the answers reflect the best available information to date.

Perhaps you'll find questions of your own here. In any event, we hope you'll find them useful.

Q. What is the fate of the drug in the body?

A. The drug is metabolized in the liver and excreted primarily in the urine.

Q. Does drug accumulation occur?

A. When recommended daily doses are administered, drug accumulation in the serum occurs only up to the seventh day. At this time, a plateau is reached and serum levels tend to remain stable with continued administration of the original dose.

Q. What is the half-life of Tranxene?

A. The serum half-life of nordiazepam, the primary metabolite of Tranxene, is approximately one day.

Q. What is the effect on blood pressure?

A. Decreases in systolic blood pressure have been observed. In our premarketing clinical studies, the only effect seen on blood pressure was the lowering of slightly elevated systolic blood pressure in some patients.

Q. Does Tranxene cause bradycardia?

A. There were no reports of bradycardia in the controlled premarketing clinical studies on Tranxene.

Q. Can urinary retention be associated with Tranxene?

A. Anti-cholinergic effects have been reported with some benzodiazepines, and therefore, it may be possible that these effects could be seen with Tranxene as well.

Q. What is the rate of excretion?

A. After a single dose, approximately fifty percent is excreted primarily in the urine in the first 24 hours. By the tenth day, 80 percent of the drug is excreted. At that point, the excretion rate was found to be about one percent per day.

Q. Has respiratory depression been seen in the studies with Tranxene?

A. There was no evidence from our premarketing clinical studies demonstrating respiratory depression with the use of recommended doses of Tranxene. However, since it is a CNS depressant, one can assume that if massive doses were ingested, respiratory depression could occur.

Q. Does Tranxene affect the SGOT level?

A. In the clinical studies, there were reports of occasional increases of SGOT level in some patients. Increases of SGOT level have been reported with other benzodiazepines.

Q. Does this mean that Tranxene is contraindicated for anyone with impaired liver function?

A. It is not a contraindication. However, as with all benzodiazepines, the usual precautions in treating patients with impaired liver function should be observed.

Q. What is the oral LD_{50}?

A. In rats the LD_{50} was 1320 mg./kg; in monkeys the LD_{50} could not be determined because of the emetic effect of large doses, but the LD_{50} exceeds 1600 mg./kg.

Q. Is it true that Tranxene can cause a decrease in hematocrit?

A. Decreases in hematocrit have been reported. A causal relationship has not been established.

Q. Can the actions of Tranxene be potentiated by the concurrent use of other drugs? What about sedation?

A. Like other benzodiazepines, the actions of Tranxene may be potentiated by the concurrent use of barbiturates, narcotics, phenothiazines, monoamine oxidase inhibitors or other antidepressants. Clinical studies have shown increased sedation with concurrent use of hypnotics.

Q. Does Tranxene have muscle relaxant properties?

A. Clinical studies in muscle relaxation have not been performed.

Q. If Tranxene is administered to elderly patients with symptoms of anxiety, what special precautions should be observed?

A. An important precaution which should be taken when prescribing Tranxene for an elderly patient is to follow the patient closely at the initiation of therapy to observe his response. In elderly or debilitated patients, it is advisable to initiate therapy at a daily dose of 7.5 mg. to 15 mg., rather than the usual recommended daily dose of 30 mg.

Therapy should take into account possible drug interactions since the elderly patient may be on other drugs.

Q. How long was Tranxene studied before being introduced?

A. The clinical investigation of Tranxene was conducted for over four years in the United States. The investigation included studies ranging from three weeks to six months.

Is Tranxene® effective?
(CLORAZEPATE DIPOTASSIUM)

Physician Evaluations:

In double-blind clinical studies, Tranxene was shown to be effective in relieving symptoms of anxiety.

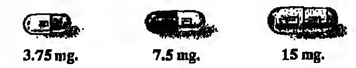
Patient Evaluations:

In most clinical studies, a series of patient self-evaluation tests were conducted under double-blind conditions before, during and after study. Improvement was recorded as a reduction in number or severity of anxiety symptoms.

Patient self-evaluations correlated well with physician evaluations—i.e. patients rated most improved by physicians tended to show greatest reduction in symptom test scores.

By both physician and patient assessment, therapy with Tranxene had a measurable effect in reducing the number and severity of symptoms.

Tranxene® is provided in 3 strengths:
CLORAZEPATE DIPOTASSIUM



3.75 mg. 7.5 mg. 15 mg.

Tranxene is administered orally in divided doses; usual daily dose is 30 mg. The dose should be adjusted gradually within the range of 15 to 60 mg., based on response of the patient. In elderly or debilitated patients, it is advisable to initiate therapy at a daily dose of 7.5 mg. to 15 mg.

In the management of anxiety... If you measure the success of the therapy by the patient's response, Tranxene
(CLORAZEPATE DIPOTASSIUM)
is an effective measure.

See last page for prescribing information.

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In the management of anxiety...
If you measure the success of the therapy by the patient's response,

Tranxene® is an effective measure.
(CLORAZEPATE DIPOTASSIUM)

Tranxene® (CLORAZEPATE DIPOTASSIUM)

DESCRIPTION: Chemically, TRANXENE (clorazepate dipotassium) is a benzodiazepine. The empirical formula is $C_{16}H_{11}ClK_2N_2O_4$; the molecular weight is 408.93.
The compound occurs as a fine, light yellow, practically odorless powder. It is insoluble in the common organic solvents, but very soluble in water. Aqueous solutions are unstable, clear, light yellow, and alkaline.

ACTIONS: Pharmacologically, TRANXENE (clorazepate dipotassium) has the characteristics of the benzodiazepines. It has depressant effects on the central nervous system. The primary metabolite, nordiazepam, reaches peak level in the blood stream at approximately 1 hour. The plasma half-life is about 1 day. The drug is metabolized in the liver and excreted primarily in the urine. (See ANIMAL AND CLINICAL PHARMACOLOGY section).

INDICATIONS: TRANXENE is indicated for the symptomatic relief of anxiety associated with anxiety neurosis, in other psychoneuroses in which anxiety symptoms are prominent features, and as an adjunct in disease states in which anxiety is manifested.

CONTRAINDICATIONS: TRANXENE (clorazepate dipotassium) is contraindicated in patients with a known hypersensitivity to the drug, and in those with acute narrow angle glaucoma.

WARNINGS: TRANXENE is not recommended for use in depressive neuroses or in psychotic reactions.

Patients on TRANXENE should be cautioned against engaging in hazardous occupations requiring mental alertness, such as operating dangerous machinery including motor vehicles.

Since TRANXENE has a central nervous system depressant effect, patients should be advised against the simultaneous use of other CNS-depressant drugs, and cautioned that the effects of alcohol may be increased.

Because of the lack of sufficient clinical experience, TRANXENE (clorazepate dipotassium) is not recommended for use in patients less than 18 years of age.

Physical and Psychological Dependence: Withdrawal symptoms (similar in character to those noted with barbiturates and alcohol) have occurred following abrupt discontinuance of clorazepate. Symptoms of nervousness, insomnia, irritability, diarrhea, muscle aches and memory impairment have followed abrupt withdrawal after long-term use of high dosage.

Caution should be observed in patients who are considered to have a psychological potential for drug dependence.

Evidence of drug dependence has been observed in dogs and rabbits which was characterized by convulsive seizures when the drug was abruptly withdrawn or the dose was reduced; the syndrome in dogs could be abolished by administration of clorazepate.

Usage in Pregnancy: Reproduction studies have been performed in rats and rabbits and there was no evidence of harm to the animal fetus. The relevance to the human is not known. Since there is no experience in pregnant women who have received this drug, safety in pregnancy has not been established.

It is assumed that TRANXENE or its metabolites is excreted in human milk. Therefore, this drug should not be given to nursing mothers.

PRECAUTIONS: In those patients in which a degree of depression accompanies the anxiety, suicidal tendencies may be present and protective measures may be required. The least amount of drug that is feasible should be available to the patient.

Patients on TRANXENE for prolonged periods should have blood counts and liver function tests periodically. The usual precautions in treating patients with impaired renal or hepatic function should also be observed.

In elderly or debilitated patients, the initial dose should be small, and increments should be made gradually, in accordence with the response of the patient, to preclude ataxia or excessive sedation.

ADVERSE REACTIONS: The side effect most frequently reported was drowsiness. Less commonly reported (in descending order of occurrence) were: dizziness, various gastrointestinal complaints, nervousness, blurred vision, dry mouth, headache, and mental confusion. Other side effects included insomnia, transient skin rashes, fatigue, ataxia, genito-urinary complaints, irritability, diplopia, depression and slurred speech.

There have been reports of abnormal liver and kidney function tests and of decrease in hematocrit.

Decrease in systolic blood pressure has been observed.

DOSAGE AND ADMINISTRATION: TRANXENE (clorazepate dipotassium) is administered orally in divided doses. The usual daily dose is 30 mg. The dose should be adjusted gradually within the range of 15 to 60 mg. daily in accordence with the response of the patient. Drowsiness may occur at the initiation of treatment and with dosage increments. In elderly or debilitated patients it is advisable to initiate treatment at a daily dose of 7.5 to 15 mg.

DRUG INTERACTIONS: If TRANXENE (clorazepate dipotassium) is to be combined with other drugs acting on the central nervous system, careful consideration should be given to the pharmacology of the agents to be employed. Animal experience indicates that TRANXENE prolongs the sleeping time after hexobarbital or after ethyl alcohol, increases the inhibitory effects of chlorpromazine, but does not exhibit monoamine oxidase inhibition. Clinical studies have shown increased sedation with concurrent hypnotic medication. The actions of the benzodiazepines may be potentiated by barbiturates, narcotics, phenothiazines, monoamine oxidase inhibitors or other anti-depressants.

If TRANXENE is used to treat anxiety associated with somatic disease states, careful attention must be paid to possible drug interaction with concomitant medication.

MANAGEMENT OF OVERDOSAGE: As in the management of overdosage with any drug, it should be borne in mind that multiple agents may have been taken.

If vomiting has not occurred spontaneously, it should be induced. Immediate gastric lavage is also recommended. General supportive care, including frequent monitoring of the vital signs and close observation of the patient, is indicated. Hypotension, though unlikely, may be controlled with Levophed® (levartarenol) or Aramine® (metaraminol). Caffeine and Sodium Benzoate injection, U.S.P. may be used to counteract central nervous system depressant effects.

There has been reported a 4½-year-old woman who took 25 capsules (187.5 mg.) of TRANXENE. Severe diarrhea and vomiting occurred, but she made an uneventful recovery without being hospitalized.

ANIMAL AND CLINICAL PHARMACOLOGY: Studies in rats and monkeys have shown a substantial difference between doses producing tranquilizing, sedative and toxic effects. In rats, conditioned avoidance response was inhibited at an oral dose of 10 mg./kg.; sedation was induced at 32 mg./kg.; the LD_{50} was 1320 mg./kg. In monkeys aggressive behavior was reduced at an oral dose of 0.25 mg./kg.; sedation (ataxia) was induced at 7.5 mg./kg.; the LD_{50} could not be determined because of the emetic effect of large doses, but the LD_{50} exceeds 1600 mg./kg.

Twenty-four dogs were given TRANXENE orally in a 22-month toxicity study; doses up to 75 mg./kg. were given. Drug-related changes occurred in the liver; weight was increased and cholestasis with minimal hepatocellular damage was found, but lobular architecture remained well preserved.

Eighteen rhesus monkeys were given oral doses of TRANXENE from 3 to 30 mg./kg. daily for 52 weeks. All treated animals remained similar to control animals. Although total leucocyte count remained within normal limits it tended to fall in the female animals on the highest dosas.

Examination of all organs revealed no alterations attributable to TRANXENE. There was no damage to liver function or structure.

Reproduction Studies: Standard studies of fertility, teratology and reproduction were conducted on rats and rabbits. Oral doses in rats up to 150 mg./kg. and in rabbits up to 15 mg./kg. produced no abnormalities in the fetuses and no impairment to fertility and reproductive capacity of adult animals attributable to TRANXENE (clorazepate dipotassium). As expected, the sedative effect of high doses interfered with care of the young by their mothers (see Use in Pregnancy).

Clinical Pharmacology: Studies in healthy men have shown that TRANXENE has depressant effects on the central nervous system. Prolonged administration of high doses (120 mg. daily as a single oral dose) was without toxic effects, and abrupt cessation of drug was not followed by serious signs or symptoms.

Absorption--Excretion: After oral administration of TRANXENE (clorazepate dipotassium), there is essentially no circulating parent drug. Nordiazepam, its primary metabolite, quickly appears in the blood stream with peak levels at about 1 hour. The plasma half-life is approximately 1 day. In 2 volunteers given 15 mg. (50 μC) of ^{14}C-Tranxene, about 80% was recovered in the urine and feces within 10 days. Excretion was primarily in the urine with about 1% excreted per day on day 10.

HOW SUPPLIED: TRANXENE (clorazepate dipotassium) is supplied as capsules, in bottles of 100.
The capsules contain:
3.75 mg (grey with white cap).....NDC 074-3417-13
7.5 mg (grey with maroon cap).....NDC 074-3418-13
15 mg (all grey).....NDC 074-3419-13

Doctors' Debate

MEDICAL TRIBUNE frequently receives extensive and well-documented communications from physicians on current subjects of controversy or those of great current medical interest. We invite contributions in these areas for presentation in this new feature.

In the January 10 issue of MEDICAL TRIBUNE, *Dr. Seymour Diamond, Assistant Professor of Neurology at the Chicago Medical School and president of the American Association for the Study of Headache, was "In Consultation" (page 5) on the subject: What's new and important in headache study? Dr. Warren F. Wilhelm, of Kansas City, Mo., then submitted a question to Dr. Diamond in a letter to the editor. Following is the question and Dr. Diamond's answer:*

QUESTION

What questions should elicit a reasonable and thorough headache history?

ANSWER

We carefully question all patients regarding the onset of their headache symptoms. Whether a headache occurred for the first time in childhood or late in life can sometimes predetermine what type of headache it is. Most migraine headaches will appear in childhood or teens and be present at least through the 50s. Headaches due to depression occur most commonly in the 40-60 age group but can occur at any age.

Location of headache: Most migraine headaches and cephalalgia due to organic disease are one-sided, while headaches due to psychogenic causes are generalized, having a hatbandlike distribution.

Frequency: A headache occurring every day most often is psychogenic, but certain persistent migraine headaches and cluster headaches can occur daily. A brain tumor will give an unrelenting headache.

Duration: A headache that is constant and never relents is most often psychogenic or due to organic disease.

Severity: Sometimes a clue because a headache due to psychogenic causes is not very severe, while migraine headache has a moderate to great severity and in cluster headache the pain is sometimes so great as to make the patient want to commit suicide.

Warning symptoms: If present in the eye, they are most often associated with migraine but may occur with certain arterial-venous anomalies. If the warning signs of the headache affect the same eye continuously and never affect the other eye, one should be suspicious of such an anomaly.

Associated symptoms: Nausea and vomiting are quite common with migraine. Cluster headache will exhibit a one-sided Horner's syndrome, with tearing of the eye, drooping of the eyelid, constriction of the pupil, and nasal congestion.

Sleep pattern: In depressive headaches there is frequent and early awakening. Anxious patients will have trouble going to sleep. Cluster patients will be awakened by the severity of the headache during the night.

I have only sketchily mentioned the points asked in your letter because of the time and space allowed. In a book written by myself and Donald J. Dalessio, M.D., entitled *The Practicing Physician's Approach to Headache*, to be published by Medcom Press in April of this year, a more elaborate discussion of these points is made. This book is written for the practicing physician as a guide to his management of the headache patient and not as strictly a reference text where the answers have to be searched out.

■

Old Problem, New View

EDITOR, MEDICAL TRIBUNE:

As a physician and former infantryman who came through two bloody battles in World War II—Leyte and Okinawa—I am familiar with human cruelty, pain, and suffering. I cannot, however, take the constant crippling and killing to which women and their unborn children are being subjected in our nation by the social injustices of protein-calorie malnutrition and the medical malpractice of dietary and salt restriction and the use of salt diuretics in pregnancy.

Metabolic toxemia of late pregnancy, low birth weight, neurologic defects, and mental deficiency are preventable socially by the elimination of poverty, and medically by sound nutritional advice and the avoidance of protein and salt restrictions and diuretic agents.

Perinatal death rates in 23 North Carolina counties from May 1, 1971, to April 30, 1972, for nonwhites were 50 per thousand or higher; in one county, Washington County, N. C., it was 126 per thousand.

It has been suggested that I should seek to win over the medical establishment in this country. I have been in constant communication with, and have been scorned by, nearly all our ob/gyn authorities, by our "nutrition experts," pediatricians, nursing authorities, pathologists, and journal editors, especially the *New England Journal of Medicine*, the *American Journal of Obstetrics & Gynecology*, *SG&O*, and *OB/GYN Survey*.

Private pharmaceutical companies are no better, as they continue to push diuretics, appetite depressants, and salt substitutes for use in pregnancy. For over six years I have had a constant battle against these practices. Worst of all are the Federal and state bureaus and institutes charged with protecting the public health, including HEW, FDA, and the USPHS.

I and others have published a wide range of statistics and many clinical studies to prove the importance of good nutrition—and the dangers of weight restriction, salt restriction, and salt diuretics for gravid women. There is an extensive and sound medical literature on this subject, available to those who wish it.

Perhaps, instead of cold statistics, a case history may make the point more vividly:

Patient M. was a small Mexican woman who followed her doctor's orders to the letter. A private ob/gyn specialist in California restricted her to *one egg and one glass of milk a week, on the grounds that there is too much salt in milk and eggs.* She was consistently advised at each prenatal visit: "Keep your weight down! Keep your weight down!" She wanted a healthy baby, so she faithfully followed her doctor's orders. Result: she gained only 14 pounds in all (from 112 to 126) and went into labor right at term. This was three months after she had been given a low-salt diet and diuretic pill to take every day; she didn't miss a day.

Her son, J.F., weighed 4 pounds, 15 ounces at birth. His blood sugar dropped to 20 mg. per cent and then later to 12 mg. per cent, and he had hypoglycemic convulsions repeatedly. The mother, after a normal blood loss at delivery, went into what her doctor termed "idiopathic shock"—which we know was caused by her hypovolemia.

The boy is obviously and grossly mentally retarded and has to attend a special school for brain-damaged children. At age 15 months he was age three to four months in development and function on the Denver Grid—head drop, crossed eyes, small head. At age 18 months he still could not pull to stand or walk.

The patient had her second son after prenatal care in my clinic. During this second pregnancy she gained 50 pounds, had two eggs and a quart of milk every day, meat, vegetables, fruits, cereals, and no salt diuretics, no dietary salt restriction. She was told on each visit: "Keep eating a good diet—salt your food *to taste!*" This second child, A., weighed 9 pounds at birth and is a perfect specimen.

Fellow American physicians, how long are we going to disregard the scientific evidence of the causal relationship of protein-calorie malnutrition, restriction of salt, and the dangerous use of salt diuretics to complications of pregnancy, fetal mortality, and damage to the newborn human infant?

TOM BREWER, M.D.
County Physician
Richmond Health Clinic
Richmond, Calif.

■

"Exercise for the Heart"

EDITOR, MEDICAL TRIBUNE:

The editorial "Exercise for the Heart—an Act of Faith," in your issue of September 27, 1972, was recently reviewed by the American Medical Association's Committee on Exercise and Physical Fitness. I have been asked, as acting chairman, to convey the substance of their reaction to you. I am also aware of the letter of Dr. Frank W. Jackson in response to this editorial, published in your issue of November 22.

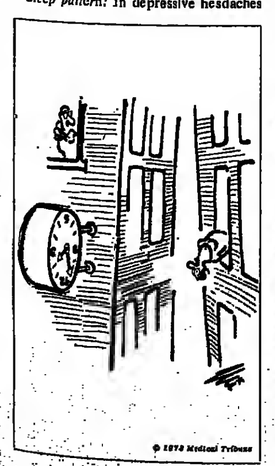
The author of your editorial cited the handbook *Exercise and the Heart, Guidelines for Exercise Programs*, edited by R. L. Morse, but failed to say that it includes many recommendations regarding the values of exercise for both the healthy and diseased heart. Instead, he chose to quote out of context three sentences from the National Heart and Lung Institute Task Force on Arteriosclerosis which appear to cast doubt on the value of exercise. The statement of Dr. Fox, which is quoted as "extending this statement of the Task Force," actually does no such thing, but does mention "beneficial effects."

Had he [the author of the editorial] referred to the booklet *Exercise Testing and Training of Apparently Healthy Individuals: A Handbook for Physicians* (American Heart Association, 1972), which was prepared by nine leading experts on rehabilitation of patients suffering from coronary artery disease (including Dr. Fox), a well-known cardiac physiologist and a nurse consultant, he could have found the following statement: "Regular, vigorous exercise enhances the quality of life, by increasing the physical capability for work and play. We believe that such exercise is an important therapeutic tool in rehabilitating patients who have angina pectoris or are recovering from myocardial infarction.... We do...encourage the widespread adoption of exercise programs tailored to the capacity and interest of individuals because of the probability that they will enrich the quality of life and, in combination with other measures, help reduce coronary risk."

Finally he quotes Francis Fuller (*A Treatise Concerning the Power of Exercise With Respect to the Animal Economy*, London, 4th Ed., 1711) entirely out of context and, in a way, to deny the whole message of Fuller's book. Fuller recommends without reservation the use of light and moderate exercise in the treatment of consumption (tuberculosis), dropsie (heart-failure), and hypochondriacal distemper (possibly manic-depressive psychosis).

I have completed the sentence which was bifurcated by your editorialist so that Fuller's true sentiment is expressed, as follows: "That the Use of Exercise does conduce very much to the Preservation of Health, that it promotes the Digestions, raises the Spirits, refreshes the Mind, and that it strengthens and relieves the whole Man, is scarcely disputed by any; but that it should prove Curative in some particular Distempers, and that too when scarce anything else will prevail, seems to obtain little credit with most People, who tho' they will give a Physician the hearing, when he recommends the frequent use of Riding, or any other sort of Exercise; yet at the bottom look upon it as a forlorn Method, and the Effects rather of his disability to relieve 'em, than of his Belief that there is any great matter in what he advises: *Thus by a negligent Diffidence they deceive themselves, and let slip the Golden Opportunities of recovering, by a diligent Struggle, what could not be procur'd by the use of Medicine alone*" (italics mine).

ALLAN J. RYAN, M.D.
Acting Chairman
Committee on Exercise
and Physical Fitness, A.M.A.



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Student, Teacher: Electronics Aids In Communication

Medical Tribune Report

LOS ANGELES—An $80,000 electronic student response system, designed to increase the efficiency of student-teacher communication, is in operation at the University of Southern California School of Medicine.

The system, recently installed in the Louis B. Mayer Medical Teaching Center, allows individual student participation and response, which would otherwise be impossible in the large-classroom environment of the 500-seat auditorium.

As questions are presented by the instructor, a push-button device on the arm of 265 seats allows a student to pick one of five possible answers. The device immediately indicates to the student whether he is right or wrong, and indicates to the instructor the percentage of the class responding, and percentage correct or incorrect for each possible answer.

An electronic scanner collects the individual student responses and feeds them to a computer, which analyzes the data and relays it to a teletype. The instructor receives an immediate printed readout with detailed data analysis of question-by-question performance by individual students and the class as a whole.

Thus, the instructor can rapidly assess student understanding of materials presented, and identify areas that need reinforcing.

This system was described as representing a marked advantage over the traditional method of assessing student comprehension by giving quizzes, which have to be graded and then returned to the students—a process entailing a long interval between presentation of the material and determination of the extent of its assimilation.

As Dr. Phil Manning, Professor of Medicine and associate dean for postgraduate medical education, noted, "the new system will allow the U.S.C. faculty to organize problem-solving sessions with active participation in large groups. These activities have previously been restricted to small groups."

The system was installed by Instructional Industries Inc., an independent affiliate of General Electric and an outgrowth of an educational systems group in the G.E. Research and Development Center.

G.I. FORUM

ROCHE

A CURRENT REVIEW OF INVESTIGATIONS IN GASTROENTEROLOGY

A kaleidoscopic entity

Gastritis . . . a disease of myriad uncertainties . . . a disease surrounded by much confusion. Very few subjects in medicine arouse so much difference of opinion.[1] Gastritis was discarded as a specific entity

in 1838 when it was discovered that rapid disintegration of gastric mucosa after death prevented confirmation that the condition had existed during life.[2,3] The advent of gastroscopy in the early 1930's, however, stirred new interest in gastritis.[2]

Today, gastritis is considered to be of many types and to have many different causes.[4] Attempts to classify the abnormality by etiologic and pathologic considerations have not been successful. To properly classify chronic superficial gastritis and differentiate it from ulcer, early carcinoma or even functional gastrointestinal disease, advanced x-ray techniques, endoscopy and biopsy are required.[3] Not infrequently, gastritis may be secondary to ulcer, pernicious anemia and the postoperative state. One of the intriguing problems as yet unresolved by histopathologic study is the relationship of acute gastritis to chronic superficial gastritis.[3,4]

Gastroscopy alone or confirming biopsy?

Part of the confusion surrounding the diagnosis of gastritis lies in the difficulty of defining its various forms, which are largely determined by the diagnostic method used.[2] Gastroscopic definitions, based on direct visual inspection, do not always correlate well with the histologic state of the mucosa—which in turn may show little relationship to symptoms.[5] While some clinicians once considered gastroscopy to be the best method of diagnosing chronic gastritis,[3] most insist that the visual method be confirmed by biopsy.[2,4] The consensus is that despite the possibility of sampling error due to the limited area examined, histologic findings are the *sine qua non* in the classification of chronic gastritis.[2]

Does aspirin irritate normal G.I. mucosa?

Almost always. Some view aspirin irritation of gastric mucosa as a general phenomenon rather than one restricted to hypersensitive persons.[6] Others suspect an individual sensitivity that develops only in particular circumstances.[7] Wide variations have been noted in individual tolerance of gastric mucosa to circulating salicylates.[4] One investigator suggests that those who are immune to aspirin irritation may have a high replacement of gastric epithelial cells.[8]

Does gastritis precede ulcer or vice versa?

In more than 40 per cent of gastric ulcers, gastritis either appears as a border of swelling around the ulcer or involves all of the gastric mucosa.[3] But the question of which came first—the ulcer or the gastritis—has never been settled. An old theory which still has its adherents regards the gastritis as secondary to the stomach ulcer.[9] This group saw it as an inflammatory reaction spreading from the ulcer site and usually called it "zonal gastritis." However, recent work using biopsy specimens obtained during gastroscopy would seem to refute this belief.[10] The persistence of superficial or atrophic gastritis after a gastric ulcer has healed would imply that the ulcer may be secondary to gastritis.

The need to provide a comprehensive medical regimen

Such symptoms as anorexia, epigastric discomfort after meals, nausea, bloating and burning sensations may be sufficiently severe and persistent to require medical attention. Furthermore, if an acute staged gastritis is left untreated, some clinicians feel that there is risk of its leading to chronic superficial gastritis, with possible progression toward gastric atrophy.[2] Besides physical rest and respite for the inflamed stomach, some patients will very likely need respite from undue anxiety as well.

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Contraindications: Patients with glaucoma; prostatic hypertrophy and benign bladder neck obstruction; known hypersensitivity to chlordiazepoxide hydrochloride and/or clidinium bromide.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. As with all CNS-acting drugs, caution patients against hazardous occupations requiring complete mental alertness (*e.g.*, operating machinery, driving). Though physical and psychological dependence have rarely been reported on recommended doses, use caution in administering Librium (chlordiazepoxide hydrochloride) to known addiction-prone individuals or those who might increase dosage; withdrawal symptoms (including convulsions), following discontinuation of the drug and similar to those seen with barbiturates, have been reported. Use of any drug in pregnancy, lactation, or in women of childbearing age requires that its potential benefits be weighed against its possible hazards. As with all anticholinergic drugs, an inhibiting affect on lactation may occur.

Precautions: In elderly and debilitated, limit dosage to smallest effective amount to preclude development of ataxia, oversedation or confusion (not more than two capsules per day initially; increase gradually as needed and tolerated). Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (*e.g.*, excitement, stimulation and acute rage) have been reported in psychiatric patients. Employ usual precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship has not been established clinically.

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Haptene Said to Avert Allergy to Penicillin

Medical Tribune World Service

MONTREAL—Penicillin allergy can be averted by the monovalent haptene BPO-FLYS (benzylpenicilloylformyllysine), Dr. Alain de Weck, of the University of Berne, Switzerland, reported here.

Dr. de Weck, who is director of the institute of clinical immunology at the university, spoke at a conference on control of reagin-mediated hypersensitivity.

DR. DE WECK

In clinical trials, he said, allergic reaction to penicillin could be prevented in 12 out of 13 patients by the parenteral administration of BPO-FLYS 100-400 mg./day. In all patients, skin tests with BPO-FLYS at the beginning of therapy were negative, but in three cases, slightly positive skin reactions were observed after eight to 31 days of therapy.

"Those patients who were undoubtedly hypersensitive to penicillin, and who had freshly experienced clinical allergic reactions, were capable of pursuing penicillin therapy under the protection of the haptene," said Dr. de Weck.

The findings will have to be confirmed by further clinical trials, now being conducted in research centers in Switzerland, France, and West Germany, he told MEDICAL TRIBUNE. "Obviously, we are not ready yet to put this into the hands of general practitioners, because there are still some problems. But the research work is going very well."

Dr. de Weck commented that the work offers a new approach to control of the immunologic system by depression of the formation of specific antibody.

"If it is feasible to depress the formation of antibody without impairing cell-mediated immunity, then we could have new possibilities in cancer therapy," he observed.

"We have to be able to identify the tumor antigen, and in some cases this knowledge is already available."

Coauthors were Drs. C. H. Schneider, H. Spengler, O. Toffler, and S. Lazary, all of the University of Berne.

Dr. David C. Marsh, an immunologist from Johns Hopkins University, working at the Good Samaritan Hospital, Baltimore, said that his team's most recent work helped confirm the belief that allergies are genetically determined.

In exceedingly allergic patients, Dr. Marsh's group was able to demonstrate a highly significant correlation between sensitivity to the ragweed allergen Ra5 and histocompatibility antigens of the cross-reacting group (HL-A7).

Coauthors were Drs. Wilma B. Bias, Susan H. Hsu, and Lawrence Goodfriend.

WHO Experts List 6 Major Hazards To Health Found in the Environment

Medical Tribune World Service

GENEVA, SWITZERLAND—There are six major health hazards in the environment, according to World Health Organization experts meeting here. These are:

- Oxides of nitrogen, because of the unclear public health implications of these compounds in the ambient atmosphere.
- Mycotoxins, because of the possibility that such natural hazards contribute to chronic diseases, including cancer, especially in the largely agricultural countries in which warm and damp climates prevail.
- Nitrates and nitrites, because of the possibility of their ultimate conversion to nitrosamines in man and the use of nitrates in agriculture and of nitrites in foods.
- Manganese, because of its demonstrated neurotoxicity and the possibility that it may become more widely disseminated, primarily as a fuel additive.
- Polychlorinated biphenyls, because of their demonstrated toxicity and wide dissemination in water and packaging material.
- Asbestos, because of its demonstrated cancer-producing properties and widespread use for industrial, structural, and other commercial purposes.

An international program designed to develop environmental health criteria for the protection of man from this complex of environmental hazards was agreed upon at the meeting, which was under the chairmanship of Prof. Lars Friberg, of the Karolinska Institute, Sweden.

Medicine on Stamps

Berzelius

Called the father of inorganic chemistry, Baron Jöns Jakob Berzelius (1779-1848) was born in Sweden. Receiving degrees in both chemistry and medicine from the University of Uppsala, he taught pharmacy, medicine, and chemistry in Stockholm.

He discovered the elements selenium, thorium, and cerium and isolated biliverdin, a green pigment formed from bilirubin by oxidation. He introduced the present system of writing chemical symbols and formulas.

Sweden issued the stamp in 1939 to honor the 200th anniversary of the Royal Academy of Science. This year marks the 125th anniversary of Berzelius' death.

Text: Dr. Joseph Klor
Stamp: Minkus Publications, Inc., New York

Positive Cultures Seen No Bar to Early Discharge Of Tuberculosis Patients

Medical Tribune Report

GROVE, OKLA.—Follow-up studies of discharged tuberculosis patients on chemotherapy and their household contacts suggest that culture-positive patients are no more infectious than those discharged as culture-negative, the Oklahoma-Arkansas Regional Meeting of the American College of Physicians was told.

Dr. Janice J. Gunnels, of the Veterans Administration Hospital in Little Rock, Ark., conducted studies of 82 treated patients who were culture-positive at discharge and 285 of their 298 contacts and of 76 patients, culture-negative at discharge, and 243 of their 249 contacts. She indicated that it was not always possible to determine if reactors were infected before or after initiation of drugs.

Following skin testing she found that 128 of the 285 contacts of the culture-positive remained negative, 125 had reactions of 10 mm. or more, and 32 had 6-9-mm. reactions. Primary infection occurred in 34 contacts.

In the other group, 114 of the 243 evaluated contacts remained negative, 100 had reactions of 10 mm. or more, and 29 had reactions in the 6-9-mm. range. Primary infection occurred in 42 contacts.

This observation supports the practice of early discharge for culture-positive patients on chemotherapy, she concluded.

Her coauthor was Dr. Joseph H. Bates, chief of the medical service at the Veterans Administration Hospital.

Experts Hail New FDA Food-Labeling Policy

Continued from page 1

helpful to both doctor and patient by providing information that was formerly unavailable.

"Knowing about the fat content of food, whether it is polyunsaturated or not, and the caloric content will enable many patients to follow their physicians' advice more carefully," Dr. Calloway observed.

Nutritionists agreed that in managing malnutrition, cardiovascular disease, obesity, and sodium intake, the new labeling practices should close the gap between the physician's biochemical training and the existing lack of information on the foodstuffs his patients may be choosing.

"Malnutrition, the question of sodium intake, and the galloping mortality rate from cardiovascular disease," said Dr. Mayer, "are among the problems that require a definite stand on nutrition by physicians. In many cases, patients need to discuss with their physicians exactly what they have been eating, and many patients have not been doing this. This relabeling is going to make it much easier for patients to follow recommendations, and much easier for physicians to be direct about what the patient should or should not eat.

He emphasized that the new labeling practices will make it easier for physicians to learn more about nutrition.

"Now there will be no reason not to know, for example, which fats are polyunsaturated and which are not," he said. "The physician can go into his own kitchen from now on and find out for himself."

Dr. Mayer continued: "In a study which I recently did in the Boston area concerning the level of physician information on nutrition, I found out that most doctors remember their biochemistry quite well, but when it comes to applying their knowledge in a practical way to food, there is a decided gap. I think this relabeling plan will amphasize the need for more information and discussion, with benefits to both patients and doctors."

David Call, Ph.D., Professor of Food Economics, Graduate School of Nutrition, Cornell University, and a member of the FDA Commissioner's Food Advisory Committee, agreed that the new regulations may permit more specific advice from physicians and prompt more questions from patients. He noted, however, that they also may eliminate many questions now brought to physicians.

Won't Be Asking Doctors

"The specific prohibitions about saying certain things about food, if they are implemented, should clear up a lot of questions in consumers' minds so they won't be asking their doctors. They won't have to come to their doctor and say, 'Is it true that this food will cure cancer (or heart disease or something else)?' because that kind of misinformation will no longer be permitted," he said.

In addition to consumer-oriented information, such as serving size and servings per container, whenever a nutritional claim is made for a product the new regulations will require notice of calorie, protein, carbohydrate, and fat content as well as percentage of U.S. Recommended Daily Allowances (RDA) of protein, vitamins, and minerals.

The RDA replaces the Minimum Daily Requirements as the official measurements of nutritional intake. Generally, they nearly double the standards of vitamins A, B_1, B_2, niacin, B_6, folacin, pantothenic acid, B_{12}, biotin, C, D, E, and K, and calcium, chlorine, iron, magnesium, phosphorus, potassium, sodium, sulfur, copper, fluorine, iodine, manganese, and zinc.

The combination of final regulations, tentative orders, and proposals put forth by the FDA will require listing of percentages of vitamins A, C, thiamin, riboflavin, and niacin as well as calcium and iron.

Manufacturers will also be allowed, but not required, to indicate the food's content of cholesterol, sodium, and polyunsaturated, saturated, and other fatty acids.

According to an official statement, "in taking this action the FDA is not taking a position on the scientific debate surrounding the role of fat consumption in heart disease. Consumers, however, should be able to identify foods for inclusion in physician-recommended fat-modified diets."

The new regulations would define as a dietary supplement any item containing 50-150 per cent of the U.S. RDA of vitamins and minerals, require disclosure of their contents, and prohibit claims that they can prevent, cure, or treat disease. Any product exceeding 150 per cent of the RDA must be labeled and marketed as a drug.

Based on '68-70 Hearings

The U.S. RDA and supplemental dietary regulations are based on the Special Dietary Food Hearings conducted by the FDA during 1968-70.

According to the head of the FDA, Dr. Charles C. Edwards, the regulations will implement virtually all the labeling recommendations of the White House Conference on Food, Nutrition, and Health.

He stressed that professionals must help consumers "understand and utilize the new labeling information."

"As the program gets under way," he said, "labels will begin routinely bearing information never before seen by the average consumer. It is important for all of us to make every effort to inform consumers on how to use this new labeling to the benefit of themselves and their families."

All of the FDA's actions are scheduled to be finalized within six months of their appearance in the *Federal Register* on January 19.

Jackson, With History Of Violence, Is Calmed By Amphetamine Therapy

Continued from page 1

peared within an hour, Dr. Corson reported. With continued amphetamine therapy, Jackson welcomed the approach of laboratory personnel, even whimpering for further petting. He became nonaggressive with dogs previously attacked, and showed rapid learning in the pavlovian conditioning situation.

After six weeks of drug-facilitated psychosocial therapy, medication was withdrawn. Although the hyperkinesis reappeared, there was no recurrence of violent behavior and the dog did not forget what had been learned in the conditioning experiments.

"This has interesting implications for the learning of hyperkinetic or violent children in school under the influence of stimulants," Dr. Corson said. "Insofar as it is valid to extrapolate from animals to humans, this suggests that what such children learn in school while medicated with amphetamine they would tend to retain later."

Low Hyperkinesis Persisted

An additional two months of amphetamine and psychosocial therapy for the dog brought a reduction in the hyperkinesis that persisted even after withdrawal of the drug.

Dr. Corson found that dosages required for control of violent behavior were the same for dextroamphetamine or the levo isomer. By contrast, the control of hyperkinesis required four times as much levoamphetamine as dextroamphetamine.

The differential effects of the two isomers, he commented, "would suggest the involvement of a dopaminergic system in violent behavior and primarily a noradrenergic system in hyperkinesis."

The investigator noted that genetic factors may have played a role in the behavior of this dog. All of its five littermates exhibited similar behavior patterns.

Care for Zoo Animals

Pathologists from New York Medical College, currently conducting comparative studies of diseases shared by man and beast, will provide medical care for N.Y.C. zoo animals that are ill or injured. Above, Edward Garner, D.V.M., examines chimp at Central Park Zoo.

Type of Histoplasmosis Needs No Treatment

Medical Tribune Report

CHICAGO—Progressive multinodular pulmonary histoplasmosis is a distinct clinical and radiological entity in the spectrum of histoplasmosis that has not been previously emphasized, according to a study of five untreated patients reported here by a team of Canadian investigators.

"On the basis of our experience," Drs. Max J. Palayew and Harold Frank, of Jewish General Hospital, Montreal, told the 58th annual meeting of the Radiological Society of North America, "it would appear that therapy is unwarranted."

Noting that four of the patients were followed from seven to nine years and the fifth for four years without therapy, they reported that "they are all well and asymptomatic." Surgery was performed in one patient for an initial solitary enlarging noncalcified nodule and in another patient to exclude metastatic spread of thyroid malignancy.

The investigators commented that their experience "would tend to support a most conservative approach to the patient with multiple histoplasmomas even in the face of growth and/or cavitation."

They emphasized that lack of awareness of this entity can lead to the needless risks of thoracotomy and/or amphotericin B therapy.

Discussing the radiologic findings, the physicians said that, regardless of the initial radiologic presentation, all five patients subsequently developed multinodular parenchymal changes; two developed typical central calcification, and two showed cavitation at varying stages of their evolution. Nodules also showed both increase and decrease in size during follow-up examination. Some disappeared while others were developing.

"This variable radiologic picture remains somewhat puzzling in terms of pathogenesis," Drs. Palayew and Frank said.

The diagnosis, they observed, obviously cannot be made on radiologic grounds alone but requires either histologic, mycologic, or serologic confirmation. In their five patients, the diagnosis was based on histologic findings in two and on serologic evidence in three.

They added that the "value of tomography in demonstrating multiple pulmonary nodules cannot be overemphasized. In some of our patients, when several nodules were seen on routine chest films, tomography showed numerous nodules."

Doppler Ultrasound Valuable In Detecting Venous Occlusion

Medical Tribune Report

PHILADELPHIA—Doppler ultrasound is an "excellent" device for the detection of lower limb venous occlusion and is comparable in effectiveness with iodine[125] fibrinogen test, a relatively new diagnostic procedure, investigators from the Oklahoma City VA Hospital reported here.

A study of 52 patients demonstrated that there is no statistical difference between the two procedures in sensitivity in the detection of deep venous thrombosis, the investigators told the 17th annual meeting of the American Institute of Ultrasound in Medicine. Doppler ultrasound, however, has the advantage of being atraumatic, rapidly done, and not subject to interference from previous isotopic procedures, said Harold Poehlmann and Drs. Ross E. Brown and James M. Hartsuck.

In the I^{125} fibrinogen test, they explained, the agent is administered intravenously and after a two-hour interval uptake counts are made with a scintillation counter. The probe is placed over a minimum of seven marked points following the deep venous drainage in the leg. An abnormal test is determined by a 20 per cent increase in counts at two consecutive points on the same leg on the same day and sustained for two days.

In the Doppler technique, they said, spontaneous venous flow is detected when the transducer is placed over a vein in the leg and this results in a cyclic blowing sound regulated by the respiratory cycle.

Flow Velocity Increased

"When a group of muscles are contracted or are squeezed, an additional quantity of blood flows into the venous system, momentarily increasing the velocity of venous flow," they remarked. "The sound derived from the increased velocity is called augmented flow. This is present when the deep venous system is patent.

"When the system is occluded, there is no augmented flow, an indication of venous obstructive disease."

The 52 patients were seen on seven consecutive days with a total of 728 limbs examined, they reported.

Three limbs were found with no augmented venous sound and abnormal I^{125} tests were also noted. Venography confirmed these results.

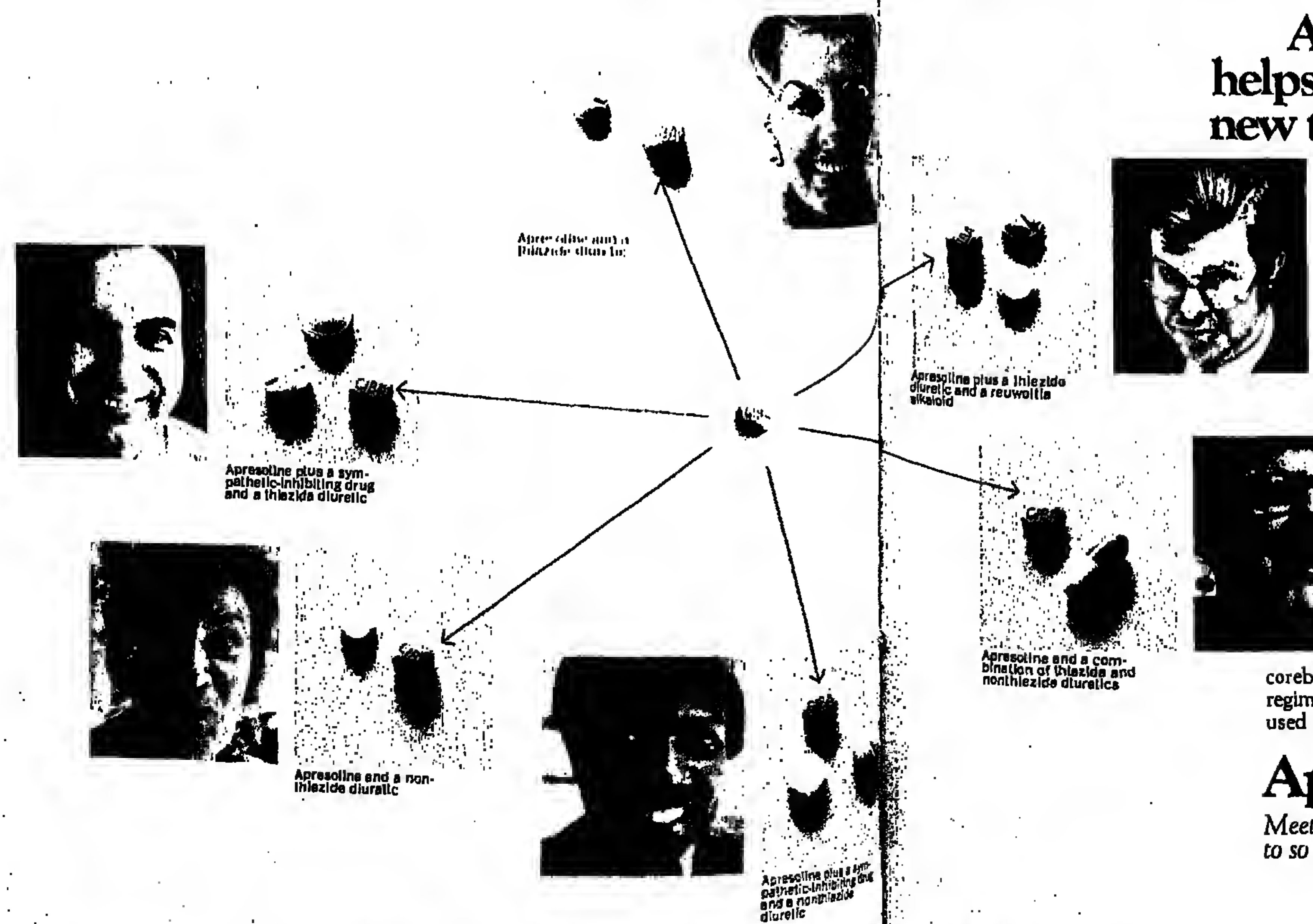
Four limbs were found where the augmented venous sounds were not as loud as would normally be expected from a totally unobstructed vein. Of these four limbs, two were confirmed by I^{125} as being equivocal, it was reported. The two other limbs were not followed by I^{125} because of interference from a liver scan given during the same period. No venography was performed, and the patients completed an uneventful postoperative recovery.

Of the remaining limbs, the investigators reported, 721 were normal on Doppler examination but two yielded equivocal results with I^{125}; these results, however, returned to within normal limits by the end of seven days.

An apparent disadvantage of Doppler ultrasound, the investigators noted, "is that all of the deep venous system on the calf must be occluded before the augmented flow is lost or the popliteal must be involved."

The three main veins in the calf, they pointed out, are the anterior tibial, posterior tibial, and peroneal. "If a single vein is occluded, the augmented sound may be heard, although it may be diminished. Once the thrombosis has progressed from a single vein into the popliteal, the augmented sound will be lost."

Apresoline... an antihypertensive idea whose time has come
(hydralazine)



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Usage in Pregnancy
Although there has been no adverse experience with Apresoline in pregnancy, the drug should be used only when, in the judgment of the physician, it is deemed essential to the welfare of the patient.
PRECAUTIONS
Use cautiously in suspected coronary artery or other cardiovascular diseases, cerebral vascular accidents, and advanced renal damage. Postural hypotension may occur, and the pressor response to epinephrine may be reduced. Peripheral neuritis, evidenced by paresthesias, numbness, and tingling, has been observed. Published evidence suggests an antipyridoxine effect and addition of pyridoxine to the regimen if symptoms develop. Blood dyscrasias, consisting of reduction in hemoglobin and red cell count, leukopenia, agranulocytosis, and purpura, have been reported rarely. If such abnormalities develop, discontinue therapy. Periodic blood counts are advised during prolonged therapy.
ADVERSE REACTIONS
Common: Headache; palpitations; anorexia; nausea; vomiting; diarrhea; tachycardia; angina pectoris. *Less frequent:* Nasal congestion; flushing; lacrimation; conjunctivitis; peripheral neuritis, evidenced by paresthesias, numbness, and tingling; edema; dizziness; tremors; muscle cramps; psychotic reactions characterized by depression, disorientation, or anxiety; hypersensitivity (including rash, urticaria, pruritus, fever, chills, arthralgia, eosinophilia, and, rarely, hepatitis); constipation; difficulty in micturition; dyspnea; paralytic ileus; lymphadenopathy; splenomegaly; blood dyscrasias, consisting of reduction in hemoglobin and red cell count, leukopenia, agranulocytosis, and purpura.
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sudsing antibacterial soapless skin cleanser
pHisoHex contains a colloidal dispersion of hexachlorophene 3% in a stable emulsion consisting of emsulon (sodium octylphenoxyethoxyethyl ether sulfonate) 50%, petrolatum 7%, lanolin cholesterols 0.7%, methylcellulose, polyethylene glycol, polyethylene glycol monostearate, lauryl myristyl diethanolamide, sodium benzoate, and water. pH 15.0 to 6.0) is adjusted with hydrochloric acid. All ingredients w/w.
Actions: pHisoHex has bacteriostatic action against staphylococci and other gram-positive bacteria. Cumulative antibacterial action develops with repeated use.
Indications: pHisoHex is indicated for use as a surgical scrub and a bacteriostatic skin cleanser. It may also be used for washing to control an outbreak of gram-positive infection in the nursery when good hospital practice has been inadequate as a total program of infection control. It should be used only as long as necessary for infection control.
Contraindications: pHisoHex should not be used on burned or denuded skin. It should not be used as an occlusive dressing, wet pack, or lotion. It should not be used routinely for prophylactic total body bathing. It should not be used as a vaginal pack or tampon, or on any mucous membranes. pHisoHex should not be used on persons with sensitivity to any of its components. It should not be used on persons who have demonstrated primary light sensitivity to halogenated phenol derivatives because of the possibility of cross-sensitivity to hexachlorophene.
Warnings: *Rinse thoroughly after use*, especially from sensitive areas such as the scrotum and perineum.
If left in contact with burned or denuded skin or mucous membranes, sufficient hexachlorophene may be absorbed to cause toxic symptoms. Infants, especially premature infants or those with dermatoses, are particularly susceptible to hexachlorophene absorption.
Systemic toxicity may be manifested by signs of stimulation (irritation of the central nervous system, sometimes with convulsions. *pHisoHex should be discontinued promptly if signs or symptoms of cerebral irritability occur.* Experimental and clinical evidence indicates that hexachlorophene toxicity is reversible.
In a small number of reported cases, fatal intoxications from hexachlorophene have occurred. These cases include misuse of 3% hexachlorophene on burned skin or exposure to a powder accidentally containing approximately 6.5% hexachlorophene. Examinations of brain tissue in some of these cases revealed vacuolization like that which can be produced in newborn experimental animals following repeated topical application of 3% hexachlorophene for 5th days.
pHisoHex is intended for external use only. If swallowed, pHisoHex is harmful especially to infants and children. pHisoHex should not be poured into measuring cups, medicine bottles, or similar containers since it may be mistaken for baby formula or other medications.
Precautions: pHisoHex suds that get into the eyes accidentally during washing should be rinsed out promptly and thoroughly.
Adverse Reactions: Dermatitis and photosensitivity. Sensitivity to hexachlorophene is rare; however, persons who have developed photoallergy to similar compounds also may become sensitive to hexachlorophene.
In persons with highly sensitive skin, the use of pHisoHex may at times produce a reaction characterized by redness and/or mild scaling or dryness, especially when it is combined with such mechanical factors as excessive rubbing or exposure to heat or cold.
Treatment of Accidental Ingestion: The accidental ingestion of pHisoHex in amounts from 1 to 4 oz. has caused anorexia, vomiting, abdominal cramps, diarrhea, dehydration, convulsions, hypotension and shock, and in several reported instances, fatalities. (See Prescribing Information for detailed treatment.)
How Supplied: pHisoHex is available in unbreakable plastic squeeze bottles of 5 ounces, 1 pint, and in plastic bottles of 1 gallon.
For detailed DIRECTIONS, consult Prescribing Information.

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Bravo, Commissioner!

We have on previous occasions congratulated Dr. Charles C. Edwards, Commissioner of Food and Drugs, and we do so again, now that the FDA is introducing the changes in good labeling practices that will permit consumers to know the content of processed foods (see page 1). On this occasion we can clearly show the difference in the position taken by the FDA under Dr. Edwards' leadership from that assumed six years ago under another commissioner. We reprint the following editorial that was published in MEDICAL TRIBUNE, *May 22, 1967.*

The FDA and Fats in the Diet

THE PROFESSOR OF NUTRITION at the Harvard School of Public Health, Jean Mayer, Ph.D., D.Sc., sharply revived the question of labeling edible fats, oils, and fatty foods to show percentages of unsaturated and saturated fatty acids. In his address before the Division of Environmental Sciences of the New York Academy of Sciences, Dr. Mayer went further than that. He said, "It is unfortunate that our Federal Government, which has already dragged its feet to a scandalous extent as regards action against cigarette smoking, is equally negligent as regards saturated fat, with the Food and Drug Administration and its new director refusing to allow advertising claims which would emphasize the cardiovascular advantages of polyunsaturated fatty acids and, therefore, encourage industrial concerns to change their processing customs to encourage a change in the nature of the fats used."

For many years an association has been noted between the incidence of coronary artery disease and the levels of blood cholesterol and other lipids, and these in turn have been related to the dietary intake of particular fats. In 1961 the American Heart Association called for "reasonable substitution" of polyunsaturated for saturated fats, because this would help reduce blood cholesterol levels and because the incidence of coronary artery disease in our country is unreasonably high. In 1965, the A.H.A. made stronger recommendations. It noted that "in most persons, but not all, the level of cholesterol and other fats in the blood can be decreased and maintained at a lower value by conscientious and long-term adherence to a suitable diet." The A.H.A. urged for most people a significantly decreased intake of saturated fat and a significantly increased intake of polyunsaturated fat, with polyunsaturated fats being substituted for saturated fats in the diet wherever possible.

But in 1959 the FDA ruled that labeling of a food that implied that consumption of polyunsaturated fats could prevent or treat heart or artery disease was a misdemeanor. In 1965 the FDA invited interested parties to file statements on a proposed regulation that a food represented as of special dietary use in the intake of fatty acids bear a label listing accurately the number of grams of saturated, monounsaturated, and polyunsaturated fatty acids contained in an ordinary serving and in 100 Gm. This was done at the request of the American Diabetes Association and six prominent clinicians in heart disease and nutrition.

Early in 1966 Dr. James L. Goddard, Food and Drug Commissioner, rejected the proposal and stated that it was the agency's position that manipulation of blood cholesterol levels through diet is not "conclusively accepted by scientists as the best way to prevent, treat, or control heart or artery disease." It is this ruling of Commissioner Goddard that Dr. Mayer objects to. We object to it, too, and find it disturbing that the FDA has in its power to make and enforce such a decision in the face of contrary opinion based on abundant research by expert investigators and physicians.

Cigarettes and Women

ACCORDING TO A STUDY by Dr. David M. Spain and his colleagues, 62 per cent of women dying from coronary heart disease were heavy cigarette smokers; this was true of only 28 per cent of women dying from other causes. The incidence of lung cancer among women has also risen with an increase in their smoking habits.

And now the latest annual report to Congress by the Public Health Service on the consequences of smoking emphasizes that "12 retrospective and prospective studies have revealed a statistically significant relationship between cigarette smoking and an elevated mortality risk among the infants of smokers." There is "a strong probably causal association between cigarette smoking and higher late fetal and infant mortality among smokers' infants."

We vigorously support equal rights for women, but we also recognize and cherish what the French so aptly called *la petite différence*. This risk to the fetus falls in that area, but we call upon women to discontinue smoking not for that reason alone.

The Hyperkinetic Dog

EXPERIMENTAL QUOTE: *"We do not wish to leave the impression that all violent behavior can be eliminated with the help of drug therapy. Psychosocial therapy should be tried before any drug administration is instituted. Our studies suggest that in some types of violent behavior which cannot be controlled by any form of psychosocial therapy, certain drugs may supply some neurotransmitters which then enable the organism to respond to other behavior-modification methods."* (Samuel A. Corson, Ph.D., Professor of Psychiatry, Ohio State University College of Medicine at the annual meeting of the A.A.A.S.; see page 1.)

"Dr. Parker, internist; Dr. Walski, nephritis specialist; and Mr. Forshelin, our expert on insurance forms."

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READERS CONTRIBUTE

A Point on Acupuncture

Editor, MEDICAL TRIBUNE:

During a recent visit to the West Coast, I heard many stories about the successes of Chinese doctors in the practice of acupuncture. Regrettably, there is evidently little effort on the part of the Chinese acupuncture doctors to join the medical community in America by passing state boards and obtaining full medical licenses —regrettably, because the art of acupuncture appears to offer something new and scientifically curious. Who but the Chinese who are already here should be able to give us valuable teaching on the subject?

B. RODANSKY, M.D.
Chicago, Ill.

■

1. Grow Tobacco
2. Don't Smoke

Editor, MEDICAL TRIBUNE:

Praise be to the American Public Health Association for a valiant effort to stop or curtail smoking. The relationship between coronary artery disease and tobacco has been suspected as a leading or contributory factor for decades. Tobacco has also been suspected in Buerger's disease, hypertension, chronic (smokers') bronchitis, emphysema, gastritis, ulcer, and other conditions, wherein elimination of smoking appears beneficial.

Spot TV, radio, and newspaper ads say: "The Surgeon-General has determined that cigarette smoking is harmful to your health." It would be more correct to state: "The Surgeon-General *warns* that cigarette smoking *can* be harmful to your health." Despite the surgeon-general, tobacco growers still receive government farm support.

ERICH KAUFMANN, M.D.
Scottsdale, Ariz.

■

FDA—Drug Regulation

Editor, MEDICAL TRIBUNE:

I was amused to read Dr. Charles C. Edwards' response to the question whether his administration was regulating drugs or doctors [interview, MEDICAL TRIBUNE, January 10].

In attempting to examine his response logically, we must reason that even the FDA cannot regulate drug efficacy, mode of action, chemical composition, side effects, etc. The FDA can and does regulate its manufacture, purity, and distribution.

When you regulate its use, you *de facto* regulate the individual who effects its ultimate distribution to the consumer—the prescribing physician. A rose remains a rose despite Dr. Edwards' hedging. Is it so painful to present the truth?

Does Dr. Edwards believe that his organization's "expertise" with respect to the utilization of drugs would be banned as evidence in any court in this country? I think not.

The indirect threat of economic sanction by litigation is a technique well-known in government circles, and with informed consumers and their legal counsel ready to take up the cause at a moment's notice, the FDA need take no action other than "regulating the drug." The credibility gap persists—only the camouflage wears thin.

C. EARL HILL, M.D.
University of Maryland

■

The Vas Rejoined

Editor, MEDICAL TRIBUNE:

In a recent issue you reported that vasectomy "has become an increasingly popular and widely accepted means of birth control in the United States." This is indeed true. Vasectomies increased from about 50,000 yearly during the 1960s to some 750,000 in 1970.

Your article then rather deplored the number of people who thought that vasectomies were reversible and suggested that "medical and allied professions make certain that persons seeking a vasectomy fully understand the permanency of the operation."

No man or woman considering a sterilization should assume that it could be easily reversed, and must think of it in terms of being permanent. However, it should also be pointed out that, depending on the techniques used for the sterilization and on the very special skills of the surgeon performing the reversal and also, perhaps, on luck, it is possible to restore fertility by rejoining the severed tubes or vas. It would not be fair, therefore, to disapprove of sterilization on the grounds that it is totally irreversible.

In my book on sterilization I quote Donald A. Goodwin, M.D., head of urology at the U.C.L.A. Medical Center, as saying that in the hands of experienced and well-trained urologists one should expect to achieve up to 90 per cent success in restoring fertility following vasectomy. Dr. John W. Dorsey of Long Beach reported a success of over 80 per cent in a series of over 100 cases and Elmer Bell of Los Angeles has reported 85 per cent success in rejoining the vas so that sperm cells once again appeared in the semen.

H. CURTIS WOOD, JR., M.D.
Fort Washington, Pa.

Editor's Note: The Supreme Court decision on abortion has dimmed the significance of controversy. Correspondence on the subject must therefore now be closed.

Gut Flora Thought to Hold Key To Diet–Colon Cancer Relation

Medical Tribune Report

ATLANTA, GA.—A theory that relates cancer of the colon to diet—with the gut bacterial flora serving as a "vital intermediary" in the relationship—was outlined by a British investigator here at an International Conference on Anaerobic Bacteria.

Dr. M. J. Hill, of the Wright-Fleming Institute, St. Mary's Hospital Medical School, London, said the search for a dietary factor in colon cancer has been under way since 1967, when epidemiologic studies showed a much lower incidence of this malignancy in Japan, East Africa, and India than in Western Europe or North America.

Various research groups, he added, have suggested that such differences in incidence might derive from different intakes of food elements ranging from fat and protein to refined carbohydrate and fiber.

"Our studies, based on World Health Organization statistics, show the incidence of colon cancer to be strongly correlated with the amount of dietary fat and animal protein and not at all with dietary fiber," Dr. Hill told the conference, which was sponsored by the Center for Disease Control, the Upjohn Company, and Emory University.

Correlation Coefficients Listed

The correlation coefficient between bound fat and incidence of colon cancer cited by Dr. Hill was a high 0.88; a strong correlation was also found between bound fat and breast cancer (correlation coefficient 0.80). The correlation coefficient between animal protein and incidence of colon cancer was 0.87 (0.79 for breast cancer).

By contrast, dietary fiber appeared to have little or no correlation with either form of cancer, and refined sugar showed coefficients of only 0.32 and 0.50.

Noting that the previous hunt for preformed carcinogens in the diet had not produced any adequate explanation for the diet–colon cancer correlation, Dr. Hill said he and coinvestigators began with the hypothesis that the gut bacteria might play a role as intermediaries. They postulated that:

- Cancer of the colon is caused by production of carcinogens and/or carcinogens by gut bacteria from dietary components or from intestinal secretions produced in response to the diet.
- The nature of the diet affects the composition of the intestinal bacterial flora and determines the substrates available for bacterial metabolism.
- Since the diet controls the intestinal flora, the substrates available for carcinogen production, and also the physiologic conditions within the gut, this would explain the correlation between diet and the incidence of colon cancer.

Fat was chosen as the dietary component most likely to be concerned, Dr. Hill pointed out, because the amount of dietary fat determines the concentration of steroids in feces "and many acid steroids have been claimed to be carcinogenic."

The team's working hypothesis was that the amount of dietary fat determines both the concentration of bile acids and cholesterol in the large intestine and the bacterial flora acting on these steroids and that bacteria can produce carcinogens and/or carcinogens from the biliary steroids.

Fecal specimens from people living in areas of high and low incidence of colon cancer were then examined for bacterial flora and steroid content.

When the two types of specimens were compared, the investigators found that feces from people in low-incidence areas had fewer anaerobic gram-negative Bacteroides organisms and more enterococci than did feces from people in high-incidence areas. Also, specimens from the low-incidence area had a much smaller amount of fecal steroid (both acid and neutral) and such fecal steroids were much less bacterially degraded.

"Considering these results in the light of our working hypothesis," Dr. Hill said, "the amount of presumed substrate available for carcinogen production was greater in the high-risk groups and the degree of bacterial action was also greater."

Chemical studies have yielded support for the theory that bacteria can produce a carcinogen from biliary steroids and possibly from amino acids, according to Dr. Hill.

One area of investigation has been the bile acids synthesized in the liver—cholic acid and chenodeoxycholic acid. Bacterial dehydroxylation of cholic acid produces deoxycholic acid, a substance considered carcinogenic by some scientists.

Although its apparent carcinogenicity in rats has been disputed, Dr. Hill commented that "there is an extremely good correlation between the mean fecal concentration of deoxycholic acid and the incidence of colon cancer" in the fecal specimens examined from low-incidence and high-incidence areas.

The possibility that bacteria might produce a polycyclic aromatic compound from the biliary steroids was also investigated by Dr. Hill's team. Four types of reaction are necessary to achieve this, he noted, and all have now been demonstrated with strains of anaerobic bacteria found in the human intestine.

He emphasized that one possible sequence of these four types of reactions yields a 17-substituted cyclopentaphenanthrene and that the carcinogenicity of these hydrocarbons has been recognized.

Amount Tied to Incidence

Preliminary studies have isolated very few organisms capable of these reactions from feces of people living in areas with a low incidence of colon cancer, but such organisms represent a "significant proportion" of the lecithinase-negative organisms isolated from people living in areas of high incidence, Dr. Hill said.

The investigator believes that the gut bacteria may be playing other intermediary roles—contributing to the urinary concentration of tryptophan metabolites, which is known to be related to the incidence of bladder cancer, and metabolizing dietary aromatic amino acids, hence producing certain urinary simple phenols known to have tumor-promoting activity.

Additionally, Dr. Hill pointed out that gut bacteria may act to promote the enterohepatic circulation of carcinogens (and their consequent retention within the body) and that activities of the gut bacterial flora may control the detoxification mechanism of the liver.

Coauthor of the report was Dr. B. S. Drasar.

On Growth Hormone

The growth progress of a four-year-old receiving human growth hormone for pituitary gland deficiency is measured by Dr. Mary Parker, of the NIH-supported clinical research center at the Washington U. School of Medicine.

Team Reduces Cord Patient Hospital Stay

Medical Tribune Report

DOWNEY, CALIF.—The Coordinated action of a team of several professionals and paraprofessionals in the treatment of patients with severe spinal cord injuries has drastically reduced their length of stay in the hospital, according to Dr. Frederick N. Elliott, assistant medical director of Rancho Los Amigos Hospital here.

If such patients are admitted within two weeks of their injury, the average length of stay is 100 days less than for those patients who are admitted after that time, after having been treated elsewhere. In terms of cost, this means a saving of some $20,000, he said.

Dr. Elliott reported that the entire team assigned to a particular patient—including student nurses, technicians, medical students, and nurses aides as well as the physician, nurses, psychologist, social worker, or physical therapist—join together in a conference on diagnosis and on frequent subsequent conferences on treatment progress and and then discharge planning.

Special emphasis is placed on the need to help both the patient and his family in readjusting to the new style of life he will have to lead because of his disability.

This team approach has made it possible to "abort the terrible depression" felt by patients and to help their families cope with the "tremendous emotional turmoil," often compounded by guilt, particularly when a young person has become paraplegic after diving into a pool or being thrown off a motorcycle.

The team member with greater rapport with the patient, regardless of his job title, is encouraged to spend as much time as possible with the patient, he added. Because so many are active on a team, which is tailor-made to the needs of each individual and thus varies in number, one or more members are always available, "and so the team can cover many more of the patients' needs."

Cared For Around Clock

Because of the comparatively large group, the patient can also be taken care of around the clock.

Special emphasis is also placed on shifting his position frequently and prevention of decubitus ulcers.

The team also sets up and measures goals, which also include prevention of loneliness as well as good physical care. "In this era we expect more than mechanical treatment of their disease," said Dr. Elliott. "We're both saving money and treating the patients much better."

Increased patient satisfaction has also gone along with increased satisfaction among the professionals and paraprofessionals, resulting in a 50 per cent reduction in turnover in team members. An added advantage has been the educational advantage to students in being so closely connected with a team.

Philippine Dogs Vaccinated In Effort to Deter Rabies

Medical Tribune World Service

MANILA—House-to-house teams have vaccinated an estimated 80 per cent of the Philippines' canine population in a country-wide campaign to stamp out rabies.

A recent study showed that an average of 250 Filipinos contract rabies each year but that from 100,000 to 150,000 persons annually require preventive vaccinations after being bitten by suspect animals.

THERAPEUTIC BRIEFS

New Use for Eosinophils

MONTREAL—Dr. Thomas Hubscher, of Montreal Children's Hospital, reported that eosinophils were found to contain a soluble factor capable of inhibiting allergic histamine release from sensitized target cells—i.e., basophils and/or mast cells.

"And man is bountifully supplied with eosinophils," he commented. "The implication is that if we can isolate this substance in pure form and synthesize it, it could be a very productive drug with minimal side effects."

He spoke at an international conference on control mechanisms in reagin-mediated hypersensitivity, held in honor of Dr. Brunn Rose, retiring allergist-in-chief of Royal Victoria Hospital and Professor of Experimental Medicine at McGill University.

Dr. Hubscher's coauthor was Dr. A. H. Eisen.

Hyperlipoproteinemia

WIESBADEN, WEST GERMANY—The likelihood of hyperlipoproteinemia in parents can be forecast from a determination of total cholesterol and beta-cholesterol levels in newborn infants, according to a German investigator.

In addition, the cholesterol levels can indicate whether the child is likely to develop the disease in later life, said Dr. Horst Wengeler, of the Heidelberg University Hospital Department of Medicine.

Total cholesterol is determined in whole serum. After ultracentrifugation, the cholesterol level is determined in the low-density plus high-density lipoprotein fraction. From this determination, the cholesterol level present in the high-density lipoprotein fraction is subtracted. This yields the beta-cholesterol level.

The disease was diagnosed in 13 of the parents of over 150 newborns in whose umbilical cord blood high total cholesterol and beta-cholesterol levels had earlier been detected, he told a meeting of the German Society for Internal Medicine.

His co-workers were Drs. Heiner Greten and Mathias Wagner.

Drug for Sex Offenders

SAN REMO, ITALY—The libido-dampening effect of cyproterone acetate is having an impact on judicial decisions in Germany and Switzerland, Dr. E. Rainer, of the Medical Division of Schering S.p. A., Milan, told MEDICAL TRIBUNE at an International Congress on Sexology.

In Switzerland, reduced sentences have been imposed in some sex offence cases when the offender agreed to undertake treatment with the drug.

"In Germany, where the sexual delinquent can get his freedom by allowing himself to be castrated, treatment with cyproterone acetate has been accepted by the Government as an analogue to the effects of castration," said Dr. Rainer.

Dr. P. Saba reported to the congress that the drug proved successful in the treatment of eight oligophrenic, cerebropathic patients suffering from hypersexuality characterized by exhibitionism, aggressivity, and continuous masturbation, at the Psychiatric Hospital of Volterra, Italy, where he is chief physician.

A Suit Over Drugs

OSAKA, JAPAN—Fifty-three victims of subacute myelooptic neuropathy have filed suit here for $4,800,000 in damages from the Japanese Government and seven pharmaceutical companies that imported, produced, or sold drugs containing iodochlorhydroxyquin, the suspected cause of their disease.

Counsel for the plaintiffs said that the suit is intended to clarify the responsibility of the Government for allowing the companies to sell the drug without confirming its safety.

Medical Tribune

HYPERTENSION BULLETIN

A CIBA SERVICE

FEBRUARY 14, 1973

PREPARED BY INTERNATIONAL MEDICAL PRESS

ORIGINS OF HYPERTENSION:

you're driving me nuts...

EXACTING, UNFAMILIAR TASKS, in which failure may mean punishment, can induce arterial hypertension in the squirrel monkey. Another set of tasks can reverse the condition in the same animal. But not all monkeys subjected to precisely the same conditions develop hypertension. Thus for them, as well as for some human beings—strong emotional effects may induce organic disease.

This report, a preliminary one from the new Specialized Center of Research in Hypertension at Harvard Medical School, casts new light on a theory first proposed by the Harvard physiologist Walter B. Cannon, who published his classic text, *Bodily Changes in Pain, Hunger, Fear, and Rage*, in 1929.

Harvard researchers are nearing their 18th month of work on a long-term collaborative study to document physiologic mechanisms that promote organic disease in subhuman primates. One physiologist gives a capsule summary of their relationship to Cannon's theories: "Cannon had a strong interest, and produced some striking leads, in various areas of psychosomatic medicine. But he had few experimental data. Our work so far finds no instance where he was completely wrong in his assumption. But our work also shows that many uncertainties remain."

The long-range goal of this study, supported by a grant from the National Heart and Lung Institute, is to find means to prevent and treat human hypertension.

Dr. A. Clifford Barger, the Hypertension Center's general director and principal investigator, points out that about 30,000,000 people in this country have some form of cardiovascular disability and the Public Health Service figures that perhaps $30.5 billion is spent annually in patient care for this disability. This includes direct costs of 5.1 billion dollars, and indirect costs of 25.4 billion dollars.

"If we were able," said Dr. Barger, "to postpone the onset of cardiovascular disease for five to 10 years—not an unreasonable goal for the next decade, provided our research momentum is maintained—the savings would be many billions of dollars."

At present, investigators of human hypertension are confronted by a complex set of unknowns, according to Dr. J. Alan Herd, Associate Professor of Physiology. To clear the way, the Harvard group is attempting to document the role of the environment—and indirectly, the emotions—in producing blood pressure elevation in laboratory monkeys.

"We chose squirrel monkeys because we needed totally naive subjects on whom we could impose a set of completely controlled and unfamiliar circumstances. Our monkeys sit alone in a chair in a very small chamber, responding to flashes of

continued on page 24

THE NATION IS TRYING to get an effective hypertension detection and treatment program under way, ultimately to cut down the massive social costs of cardiovascular disease; but there is a stricture in the channels of control; many people do not flow back for follow-up examinations. Why not?

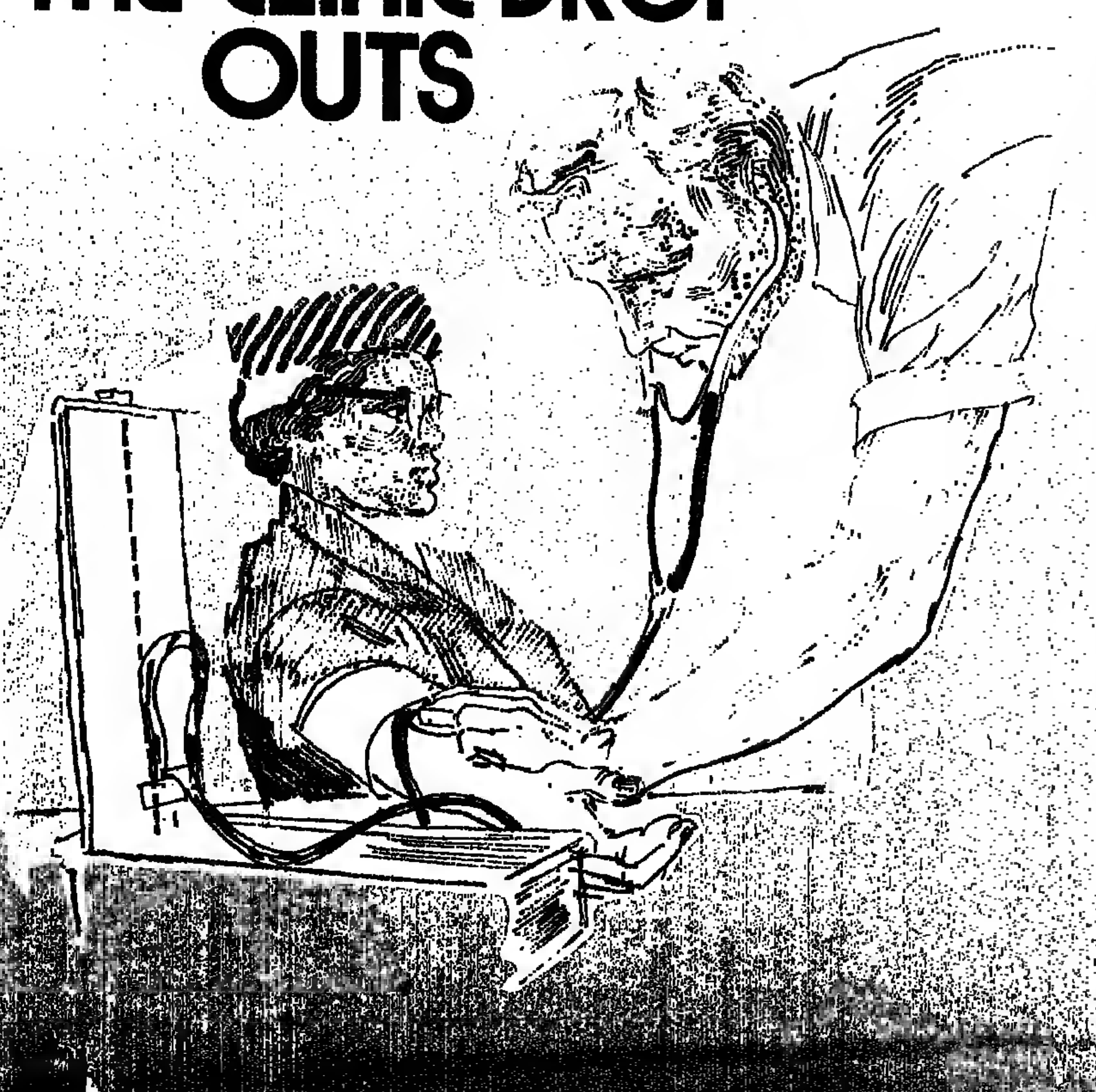
Dr. Frank A. Finnerty, chief of cardiovascular research at Georgetown University Medical Division, District of Columbia General Hospital, put the question to himself when he found that many people were dropping out of his inner-city hypertension clinics. He organized a study to find out why—and the upshot has been a tactical and structural reorganization of clinical facilities.

In 1970 the Veterans Administration Cooperative Study Group on Antihypertensive Agents found that control of blood pressure in patients with diastolic pressures ranging from 90 to 114 mm. Hg significantly lowered morbidity and mortality. The NHLI then decided to set up a cooperative, nationwide study to discover whether these findings hold true for the population at large.

D. C. General moved into the study, prepared to use its several established clinics as examination centers for the Metropolitan Washington Regional Hypertension Detection and Follow-up Program.

"The incidence of hypertension among inner-city blacks," said Dr. Finnerty, "is high, approximately 40 per cent, compared with the 12-15 per cent in the general population. It occurs earlier and is more severe. Among blacks, screening should start at age 25—and it isn't uncommon to find hypertension in teen-agers. Blacks seldom get coronaries but often get strokes. No one understands why. Strokes are as common in women as they are in men, and in the D. C. population it is not unusual to see women in their early 30s who have had strokes. We don't know whether this is a racial difference or a result of the socioeconomic stress in this area.

RETURN OF THE CLINIC DROP-OUTS



"We learned quickly that we couldn't use standard epidemiological techniques for screening. In spite of support by community leaders in the census tracts and considerable favorable publicity in the local media, house-to-house screening turned out to be dangerous. On the first day of canvassing, a female member witnessed a rape. On the second day, someone tried to rape her."

So they set up screening centers in the largest supermarkets in each of three census tracts, and 61 per cent (6,480 of 10,5[illegible]) of the residents of the tracts were screened in the markets. Nine hundred fifty-thr[illegible] were found to have pressures of 140/9[illegible] mm. Hg or higher, and these were invited to D. C. General for verification tests.

"We quickly learned that our first [illegible] a week [illegible] About [illegible] failed to show up. We were able to reduce this loss to 29 per cent by personal contact, and later to 5 per cent by making appointments within 24 to 48 hours. Each person who came to the clinic had two verification tests, and 296 were excluded because their diastolic pressures fell below 90 mm. Hg on the first or second visit. Along with dropouts, this left us with 284 patients for the study."

Dr. Finnerty and his colleagues supposed that the dropout rate was related to black suspicion of white professionals, to inadequate understanding of the seriousness of the disease, and to economic factors. But a good look exploded the assumptions.

"These patients had perfectly good reasons for not coming back to clinics. In the first place, each visit meant hours of waiting, an average of 2.5 hours before they were seen, and another 1.8 hours waiting at the pharmacy. This was on top of traveling time.

"When the patient did see the doctor, he got about seven and a half minutes of medical time. There was no real doctor-patient relationship. Not only was the doctor always in a hurry, but this is a teaching hospital and patients would see a different doctor at each visit, because of staff rotations.

"It's often assumed that clinic patients aren't motivated to get health care because they don't understand its importance. But the overwhelming percentage of the people in this study were perfectly aware that hypertension is a serious disease, and 56 per cent considered regular medical checkups important.

"We learned that the problem wasn't with the patients, but with how the patients were treated. After wasting a couple of days waiting around, patients say: 'The hell with it.' Not even a bonus system would bring them back, and the next time we'd see them would be in the emergency room with a stroke or a coronary."

Guided by the patients' complaints, procedures were changed. The Hypertension Clinic at D. C. General is kept open six days a week. Patients are seen by appointment, and every patient who is selected for long-term follow-up is assigned to a physician and a paramedical health aide. At every visit he sees the same physician and the same paramedical.

"If a patient misses an appointment, the health aide gets in touch to find out why. If it is a matter of a baby sitter or transportation, the aide finds a solution, even if it means that we arrange to pick the patient up and bring him to the clinic.

"For the most part, it's the paramedicals to whom the patients turn for information. They work under the supervision of nurses and use the doctors as consultants, but once a patient has been stabilized on medication, the aide follows the case, calling on the doctor only in the event of complications."

The Hypertension Clinic at D. C. General central clinic also offers comprehensive health care; the medical staff members act in the role of family doctors. The clinic phone is manned 24 hours a day, and there is a system for emergency services, outpatient care, and hospital admission.

"We bypassed the waiting time at the pharmacy by dispensing medication right in the clinic."

Once the clinic was operating for the benefit of the patients rather than for the convenience of the medical staff, comments Dr. Finnerty, the dropout rate fell from the high 42 per cent of 1966-1969 to 8 per cent.

In Dr. Finnerty's opinion, all clinics will have to be reorganized along these lines if "we are really going to treat and follow up patients with chronic diseases, such as hypertension." And he sees paramedicals as vital personnel in clinic staffs, contributing much more than the medical duties for which they are trained.

"Paramedicals will have to be brought into the system," he asserts. "They have to be legalized, have the right to third-party payments, and be covered by liability insurance. It's going to be difficult to persuade doctors that this concept isn't a threat to them. We can't force them to accept it. We can only show them, through repeated successful demonstrations, that paramedicals are the answer to overcrowded clinics and doctors' offices." ◼

reports from abroad

VARNA, BULGARIA—Electrosleep therapy combined with climatotherapy depresses blood lipid levels, according to a study by Prof. Dr. V. Sirakova, Director of Internal Medicine and Therapy, Institute of National Economy. Therapy depressed blood pressure, serum cholesterol, and beta-lipo-protein lipase activity in males and total lipid and triglyceride levels in females.

ULAN BATOR, MONGOLIA—A hypertension control program among various Mongolian nationals, aged 15 to 70 years, revealed: among 1,963 males, mean systolic blood pressure of 125.7, mean diastolic of 79.0; among 2,015 females, figures were 122.0 and 77.6, respectively. Diet for these peoples with common customs and traditions, is low in fruits and vegetables, high in sweets. Staple foods are meat—primarily fat mutton—and dried home-made milk products. Daily protein intake averages 109.5 Gm., 68-71 percent of which is of animal origin.

VARNA, BULGARIA—Patients with primary arterial hypertension as well as those with hypotension respond favorably to electrosleep therapy using low-frequency electric impulses, according to Prof. Dr. L. A. Studnizyna, of the Central Research Institute for Balneology and Physiotherapy, Moscow. Using this procedure, marked improvement was obtained in 96 per cent of 180 patients with hypotension and in 83 per cent of 135 with hypertension, Dr. Studnizyna reported at the third International Symposium for Electrosleep and Anesthesia.

MOSCOW—Study of arterial hypertension among 16,000 men aged 40-49 years revealed that arterial hypertension with increased systolic pressure only is not widespread: 0.7 per cent in the 40-44 year age group; 1.6 per cent in the 45-49 year group. Diastolic hypertension is more frequent: 10.1 per cent and 12.7 per cent, respectively, for the two age groups. Simultaneous rise in systolic and diastolic pressures occurred in 7.9 per cent of 40- to 44-year-olds and in 10.6 per cent of the older group.

Two ways to treat moderate hypertension and why...

why Ser-Ap-Es®

reserpine 0.1 mg
hydralazine hydrochloride 25 mg
hydrochlorothiazide 15 mg

because only Ser-Ap-Es adds hydralazine to rauwolfia-thiazide

Ser-Ap-Es does more than control blood pressure in moderate hypertension—it's a therapeutic approach that considers the whole patient. And adding hydralazine to rauwolfia-thiazide usually permits lower dosage of each component than if prescribed alone.

If there is slight renal impairment, hydralazine helps maintain or increase renal blood flow.

If the patient is stress reactive, the reserpine component should have a calming effect.

If the patient is uncooperative, Ser-Ap-Es may be a help because it contains all the medication many patients need in a single tablet.

Ser-Ap-Es should be used with caution in patients with advanced renal damage and cerebrovascular accidents. It should be discontinued at the first sign of mental depression.

why Esimil®

guanethidine monosulfate 10 mg
hydrochlorothiazide 25 mg

because Esimil offers the control-with-convenience so many hypertensives need

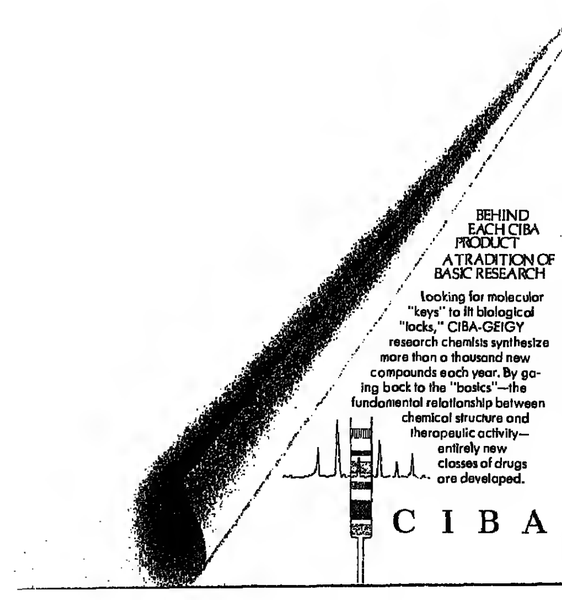
Esimil, an equally valuable yet different approach to moderate hypertension, makes sense for many patients because it anticipates future problems while helping to solve present ones.

If the patient is free of organ damage, Esimil may help keep her that way because it provides guanethidine, perhaps the most effective antihypertensive available. And effective lowering of blood pressure takes pressure off target organs.

If the patient forgets things, Esimil may make it easier to remember with once-a-day dosage, feasible in most cases.

Postural hypotension may occur with the use of Esimil, particularly while the drug is being introduced. Like all antihypertensives, Esimil should be given with caution in the presence of severe coronary insufficiency or recent myocardial infarction.

early, effective control of hypertension can save lives



Ser-Ap-Es

reserpine 0.1 mg
hydralazine hydrochloride 25 mg
hydrochlorothiazide 15 mg

Esimil®

guanethidine monosulfate 10 mg
hydrochlorothiazide 25 mg

Two ways to treat moderate hypertension

Ser-Ap-Es®

reserpine 0.1 mg
hydralazine hydrochloride 25 mg
hydrochlorothiazide 15 mg

INDICATIONS
Ser-Ap-Es is recommended for all cases of hypertension, except the mildest and the most severe.

adjust poorly to lowered blood pressure levels.
Use reserpine cautiously with digitalis and quinidine since cardiac arrhythmias have occurred with rauwolfia preparations.
Concurrent use of guanethidine and rauwolfia derivatives may cause bradycardia, mental depression, and postural hypotension.

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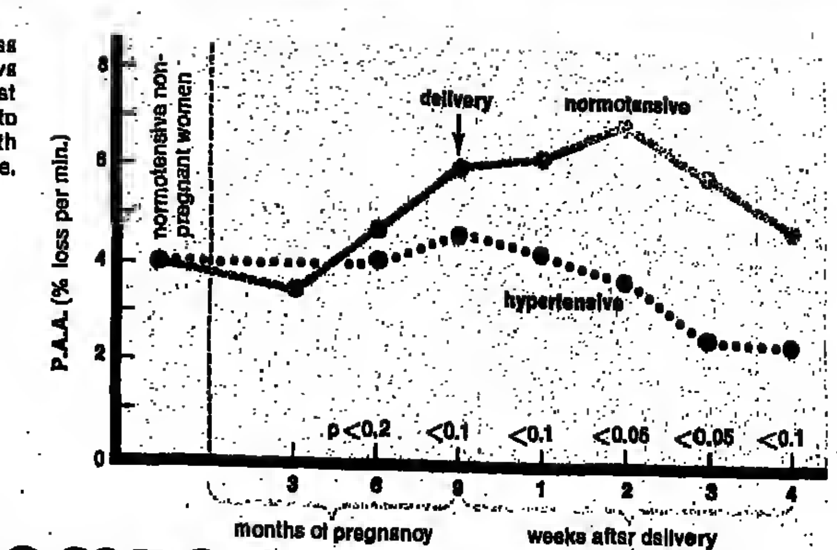


Plasma-angiotensinase activity in normotensive women rises after first trimester, but fails to increase in women with hypertensive disease.

CLUE TO PREECLAMPSIA

During the course of research into the angiotensin-renin system, three physicians at Mayo Clinic and Foundation, Rochester, Minn., found what they believe to be a clue to the pathogenesis of hypertension of pregnancy, a disease that affects 5 per cent to 25 per cent of all women, the number varying from population to population.

The investigations of Drs. Hugo R. Tapia, Carl E. Johnson and Cameron G. Strong confirmed that plasma-renin activity (PRA) and plasma-renin substrate (PRS) are significantly elevated in all pregnant women.

But in plasma angiotensinase activity (PAA), the enzymatic process of inactivation of angiotensin II—the ultimate vasopressor product of the PRA-PRS system—they found an increase only in normotensive women. Women who are susceptible of hypertensive disease failed to show an increase.

"This observation favors," they said, "an hypothesis that decreased inactivation of angiotensin II may have a role in the pathogenesis of hypertensive disease of pregnancy, the precise etiology of which is still unknown. We think we are seeing the failure of an adaptive mechanism, because all women have higher levels of PRS and PRA in pregnancy and only hypertensive women fail to show an increasing PAA."

Dr. Tapia acknowledged that a significant level of difference between PAA in normotensive women and in hypertensive women in this study of seven normotensive and six hypertensive women was not reached until two weeks after delivery. Nevertheless, through the use of an immunoassay method of measurement (so used for the first time, they believe), they were able to demonstrate that plasma angiotensinase activity in their hypertensive subjects remained level to the end of the second trimester and then, after a slight rise, sloped downward.

"Both normotensive and hypertensive women produce more angiotensinogen with the onset of pregnancy," said Dr. Tapia, "but the normal women react to these higher levels of plasma renin substrate—and consequently to higher levels of plasma angiotensin—by sharply higher angiotensinase synthesis, and consequently, they do not become hypertensive.

"In contrast, hypertensive pregnant women somehow fail to react in that way. Their plasma angiotensinase activity describes an almost flat curve."

"The purpose of our study in the long run," said Dr. Tapia, "is to find a way early in pregnancy to detect those women who are likely to develop preeclampsia. The maladaptive response to angiotensin II in the hypertensive women in our first series may prove to be helpful. The lack of an upward slope in PAA may be a presenting sign. One must follow the trend of the curve."

Dr. Tapia and his colleagues used a different method of assaying plasma angiotensinase activity than the bioassay methods usually employed.

"We used the modified Haber method of radio-immunoassay for PAA in this study. It is less variable, more sensitive."

The investigators incubated a known quantity of I^{125}-labeled angiotensin I with the plasma of the patient for two hours, measured the amount of angiotensin remaining in the incubated sample, and stated the result in terms of loss per minute.

Measurement of plasma renin activity was similarly a rate measurement, since the method used describes the speed with which renin produces angiotensin in the patient's blood in the presence of plasma renin substrate (angiotensinogen).

SPEAKING OF 78/50 110/80 BLOOD PRESSURE...

United States newspapers are increasingly reporting the blood pressure of notables, especially in critical circumstances. The *New York Times* reported the blood pressure of former President Truman when he was near death as 78/50. A few days earlier, reporting on the health of President Nixon, his personal physician, Maj. Gen. Walter R. Tkach, said his pressure reading was 110/80—down slightly from the previous year.

HYPERTENSION CLASSICS

...Poiseuille's hemodynamometer

The first blood pressure measurements ever taken were those by Stephen Hales in Britain in 1711, but it was not until more than 100 years later that his work was taken up again, by Jean Poiseuille, who in 1828 presented his mercury hemodynamometer.

Poiseuille, who, like Hales, worked with animals, concluded that "...*a molecule of blood, taken at any point of the arterial system of man, is moved by a force able to equilibrate with a column of mercury of known height....*"

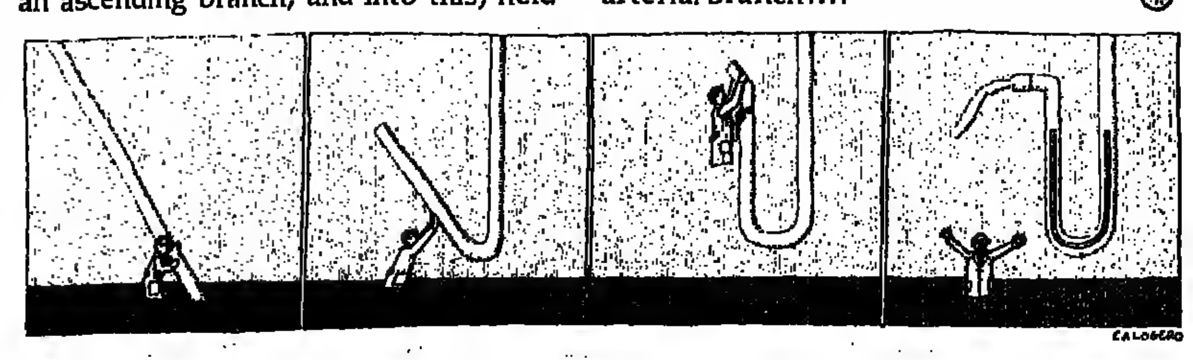
Poiseuille then established this general theorem: *"The total static force, which moves the blood in an artery, is exactly directly proportional to the square of its diameter, wherever it is located."* This theorem—Poiseuille's law—was to revolutionize hemodynamics and hydraulics.

Pursuing his investigation, he asked: *What is the force with which the heart propels the blood into the aorta?*

"To obtain this force we have but to try to obtain the height to which the blood or any other liquid, the density of which would be known to us, would rise in a vertical tube fixed in the aorta. On multiplying this height by the area of the aorta at its origin, we obtain the volume of a liquid, the weight of which provides us then *with the possible force with which the blood is moved in the aorta*, and, consequently, the action of the left ventricle of the heart in the arterial circulation."

He bent a glass tube to obtain a horizontal branch, a descending branch, and an ascending branch, and into this, held vertically, he poured his mercury, to a height about one-third down from the horizontal branch. To place this instrument "into communication with the blood, it was necessary to uncover an artery and introduce a connecting tube therein,... and the blood, passing from the artery into the tube, is mixed with subcarbonate of soda [to prevent coagulation], and transmits, through the medium of this substance, the force which propels it to the column of mercury...."

His studies led him to "conclude irrevocably that the force with which a molecule of blood moves, whether in the carotid, or in the aorta, etc., is altogether equal to that which moves the molecule in the smallest arterial branch...."



driving me nuts...

continued from page 17

light. Their response determines whether or not they will get an electric shock. Needless to say, the situation is totally foreign to these very gregarious, normally active primates, who generally run in groups of about 20 in the wild.

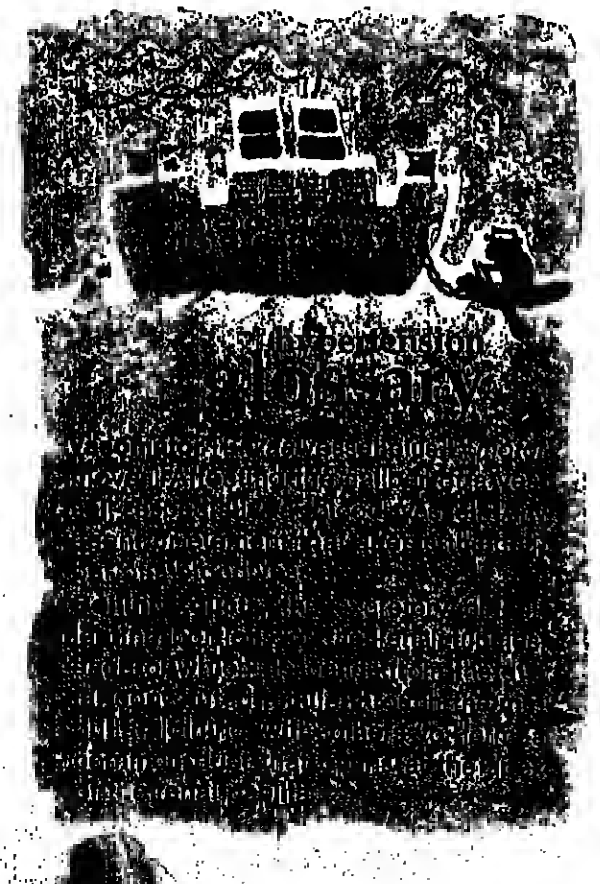
Dr. J. Alan Herd

"It is quite possible to make a human analogy here. Most of us have to curtail our gregariousness each day at work, confining ourselves to the small space of an office, or a laboratory, or a position on an assembly line. We, too, respond to cues, although they are much more subtle and complex. We respond to the alarm clock, the telephone, the lunch whistle. If we do not, there are noxious stimuli — the displeasure of superiors, no promotion, the annoyance of fellow workers."

Catheters worn continuously

In two groups of monkeys, implanted aortic catheters continuously record blood pressure levels associated with environmental cues. Preliminarily, both groups of animals are subjected to exactly the same treatment, and they show approximately the same blood pressures. Both groups wear their catheters continuously, 24 hours a day. Both live in isolation booths for a period of each day.

The change comes after this preliminary training period. In the experimental group of 11 animals, each is conditioned to press a switch key whenever a light goes on, because he learns that if he fails to switch the light off he will get an electric shock. His heart rate and arterial blood pressure increase as he goes for the key, and in a few weeks the mean pressure rise reaches 20 mm. Hg. When the animal switches the light off its blood pressure returns to base levels. But after a few months of being powerfully and continuously conditioned by environmental stimuli, an animal's mean arterial blood pressure elevation begins to persist between daily sessions. Seven control monkeys—not subjected to flashing lights and shock—have had no rises in pressure.



High pressure levels in the experimental monkeys have peaks and valleys. On days set aside for behavioral studies, arterial blood pressure is highest in the isolation booth. Afterwards, blood pressure declines to slightly lower levels. The biggest drop in arterial pressures is recorded immediately after the animal is removed from the isolation chamber. After this period of relief, the pressure gradually rises, up to the time of the next daily session in the lights cage, when it takes another spurt. From these slowly rising pressure values, it appears that the animal foresees each day's session with the lights.

To assess whether the muscular act of pressing the key raised the animal's blood pressure, the key is removed from the apparatus. The light flashes as before, and only an animal's deliberate, self-determined rise in pressure forestalls delivery of shock stimuli. The animals have soon learned to raise their blood pressure in response to the lights.

Here, too, Dr. Herd makes some cautious human analogies. "Perhaps this happens in our culture. Maybe we are rewarded not so much for performing the task, but for being crisp and responsive—or 'revved up'—in anticipation of the task. Our society tends to reward people who are aggressive, outgoing, brisk. Certainty and authority are very highly regarded."

Analogies to humans

Comparisons between human beings and squirrel monkeys are safely made on physiologic grounds, according to Dr. Herd. "Both species of primates have identical organs. So far as we know, their organs work in the same way, with similar hormone reponses of adrenal cortical steroids and adrenal medullary secretions.

"But there are some differences. Size is the most obvious. The squirrel monkey is about a foot long, and weighs less than 2 pounds. Size differences account for metabolic differences. All small primates have a higher metabolic rate than man and a slightly higher resting blood pressure."

This higher metabolic rate, says Dr. Herd, makes the squirrel monkey more typical of a particular group of people than of all people. "These monkeys are more like labile hypertensives encountered in clinical medicine than any other creature we have found. They're susceptible to a high-fat diet, and they develop hardening of the arteries just as humans do. Atherosclerotic changes in their blood vessels are microscopically indistinguishable from those in humans. So are biochemical and pathological changes. Other animals — including dogs, rabbits, rats, and guinea pigs — get hardening of the arteries, but they show different lesions in their blood vessels.

"In the lab, we feed our healthy monkeys a diet with the same composition of proteins, carbohydrates, and fats recommended for healthy humans."

But the most striking similarity between the hypertension of human beings and squirrel monkeys comes from Dr. Herd's experimental data: not all monkeys develop hypertension under pressure. Only nine out of 11 experimental animals did. Therefore, whether monkey or human, some individuals are more susceptible of hypertension in their environment than others.

This fact is reflected in statistics showing that some hard-driving executives who thoroughly enjoy their jobs are just as likely to get hypertension as their driven employees. Dr. Peter B. Dews, who was trained as a physician and surgeon at the University of Leeds in England, and who is now Stanley Cobb Professor of Psychiatry and Psychobiology in Harvard's Department of Psychiatry, says:

"It may turn out that it does not matter how blood pressure is raised—whether by pleasure or non-pleasure. It may be that the mere act of raising the pressure is what produces human hypertension. Perhaps repeated cumulative periods of high blood pressure over a period of time will do it. If so, there may be some value in searching for new prophylactic blood pressure-lowering drugs that could be given before stressful situations develop."

One way of lowering blood pressure—in the laboratory, at least—has already been found by the Harvard group. They teach squirrel monkeys to lower blood pressure in much the same way they taught them to raise it.

Does this have any human application? "I really don't know," says Dr. Dews.

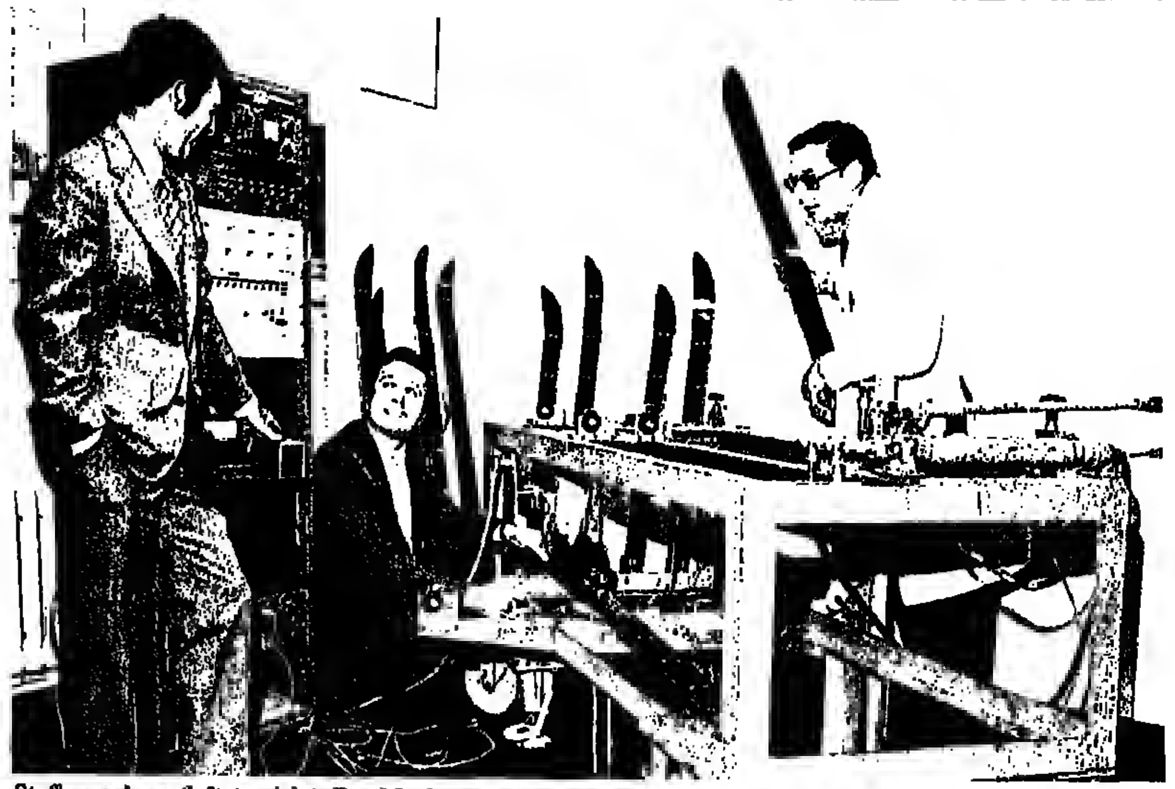
Human studies are scheduled to begin shortly at Massachusetts General Hospital under the direction of Dr. Edgard Haber, Professor of Medicine at Harvard. These studies will be grounded in the primate data accumulated thus far, plus a hint found recently in Cannon's handwritten diary: that pathologic effects of emotion may be due to failure to have normal exit in muscular movement.

Sports-Related Injuries Are Focus of Youth Unit

TREATMENT of sports-related injuries in adolescents is the prime concern of the recently established Rainbow Sports Medicine Center at Rainbow Children's Hospital, part of the University Hospitals of Cleveland. Training, research into the effectiveness of sports equipment, and methods of injury treatment and prevention in the high school athlete are other activities studied at the center, an unusual combination of medical school, hospital, and engineering school, according to Dr. Robert Mack, head of orthopedic surgery at Cleveland General Hospital and director of the center.

The center employs the science of biomechanics, the application of mechanical laws to the locomotor system, in studying the body's reactions to padding, methods of taping, equipment, and playing surfaces. Heading the biomechanical studies is Dr. Victor Frankel, director of research at the facility.

One of the courses offered by the center is for nonplaying students who participate in school athletic programs as managers and junior trainers. They learn techniques of training, exercise, and taping, allowing them a greater role in assisting their coaches and trainers. Working with the center in an advisory capacity is a board made up of Cleveland-area educators associated with athletics from the high school to the college level.



Staff members (left to right) Dr. Mack, Eugene Bahniuk, Ph.D., and Dr. Frankel demonstrating the apparatus that tests ski bindings. The center's study of the failure of most bindings to protect the skier won awards from the U.S. Ski Association and from the American Academy of Orthopedic Surgeons.

Goalie for the Cleveland Crusaders hockey team has his arm checked by Dr. Mack, team physician. Some staff members are connected with Olympics.

Young athlete, above, has his coordination tested by Dr. Frankel, who designed the testing device at the biomechanics lab at Case Western Reserve U., where he is Professor of Orthopedic Surgery and Biomedical Engineering.

Albert Burstein, D.S.M.E., of the center, photographs football player in motion. Athlete is on force-plate, a device that is used to measure the ground reaction force of the runner's take-off.

Keeping the mild hypertensive in his place

that's "Antihypertenacity" Esidrix® has it (hydrochlorothiazide)

Esidrix not only gets blood pressure down, and gets it down smoothly, but it keeps on exerting its antihypertensive effect.

Still unsurpassed as a basic diuretic-antihypertensive, Esidrix has the gradual, sustained action needed in the long-term management of mild hypertension.
We call it antihypertenacity.

And as a diuretic, Esidrix is useful in many forms of edema.

Contraindications include anuria. Use with caution in patients with impaired renal or hepatic function.

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Indications: Hypertension and edema.

Contraindications: Anuria; hypersensitivity to this or other sulfonamide-derived drugs. The routine use of diuretics in an otherwise healthy pregnant woman with or without mild edema is contraindicated and possibly hazardous.

Warnings: Use with caution in severe renal disease. In patients with renal disease, thiazides may precipitate azotemia. Cumulative effects of the drug may develop in patients with impaired renal function.

Thiazides should be used with caution in patients with impaired hepatic function or progressive liver disease, since minor alterations of fluid and electrolyte imbalance may precipitate hepatic coma.

Thiazides may be additive or potentiative of the action of other antihypertensive drugs. Potentiation occurs with ganglionic or peripheral adrenergic blocking drugs.

Sensitivity reactions may occur in patients with a history of allergy or bronchial asthma.

The possibility of exacerbation or activation of systemic lupus erythematosus has been reported.

Usage in Pregnancy

Usage of thiazides in women of childbearing age requires that the potential benefits of the drug be weighed against its possible hazards to the fetus. These hazards include fetal or neonatal jaundice, thrombocytopenia, and possibly other adverse reactions which have occurred in the adult.

Nursing Mothers

Thiazides cross the placental barrier and appear in cord blood and breast milk.

Precautions: Periodic determination of serum electrolytes to detect possible electrolyte imbalance should be performed at appropriate intervals. Observe patients for clinical signs of fluid or electrolyte imbalance (hyponatremia, hypochloremic alkalosis, and hypokalemia). Serum and urine electrolyte determinations are particularly important when the patient is vomiting excessively or receiving parenteral fluids. Medication such as digitalis may also influence serum electrolytes. Warning signs are dryness of mouth, thirst, weakness, lethargy, drowsiness, restlessness, muscle pains or cramps, muscular fatigue, hypotension, oliguria, tachycardia, and gastrointestinal disturbance such as nausea or vomiting.

Hypokalemia may develop with thiazides as with any other potent diuretic, especially during brisk diuresis, when severe cirrhosis is present, or during concomitant administration of steroids or ACTH.

Interference with adequate oral intake of electrolytes will also contribute to hypokalemia. Digitalis therapy may exaggerate metabolic effects of hypokalemia especially with reference to myocardial activity.

Any chloride deficit is generally mild and usually does not require specific treatment except under extraordinary circumstances (as in liver disease or renal disease). Dilutional hyponatremia may occur in edematous patients in hot weather; appropriate therapy is water restriction, rather than administration of salt, except in rare instances when the hyponatremia is life-threatening. In actual salt depletion, appropriate replacement is the therapy of choice.

Transient elevations in plasma calcium may occur in patients receiving thiazides, particularly in those with hyperparathyroidism. Pathological changes in the parathyroid gland have been reported in a few patients on prolonged thiazide therapy.

Hyperuricemia may occur or frank gout may be precipitated in certain patients. Insulin requirements in diabetic patients may be increased, decreased, or unchanged. Latent diabetes may become manifest during thiazide administration. Thiazide drugs may increase the responsiveness to tubocurarine. The antihypertensive effects of the drug may be enhanced in the post-sympathectomy patient. Thiazides may decrease arterial responsiveness to norepinephrine. This is not sufficient to preclude effectiveness of the pressor agent for therapeutic use.

If nitrogen retention indicates onset of progressive renal impairment, consider withholding or discontinuing diuretic therapy.

Thiazides may decrease serum PBI levels without signs of thyroid disturbance.

Adverse Reactions: *Gastrointestinal*—anorexia, gastric irritation, nausea, vomiting, cramping, diarrhea, constipation, jaundice (intrahepatic cholestatic), pancreatitis. *Central Nervous System*—dizziness, vertigo, paresthesias, headache, xanthopsia. *Dermatologic-Hypersensitivity*—purpura, photosensitivity, rash, urticaria, necrotizing angiitis, Stevens-Johnson syndrome, and other hypersensitivity reactions. *Hematologic*—leukopenia, agranulocytosis, thrombocytopenia, aplastic anemia. *Cardiovascular*—orthostatic hypotension may occur and may be potentiated by alcohol, barbiturates, or narcotics. *Other*—hyperglycemia, glycosuria, hyperuricemia, muscle spasm, weakness, restlessness. Whenever adverse reactions are moderate or severe, reduce dosage or withdraw therapy.

Dosage: Individualize dosage by titrating for maximum therapeutic response at the lowest possible dose.

Hypertension: *Initial*—Usual dose 75 mg daily. *Maintenance*—After a week dosage may be adjusted downward to as little as 25 mg or upward to as much as 100 mg daily. *Combined therapy*—When necessary, other antihypertensives may be added gradually and with caution because of the potentiating effect of this drug. Dosages of ganglionic blockers should be halved.

Edema: *Initial*—25 to 200 mg daily for several days. *Maintenance*—25 to 100 mg daily or intermittently. Refractory patients may require up to 200 mg daily.

Supplied: *Tablets*, 50 mg (yellow, scored) and 25 mg (pink, scored); bottles of 100, 1000 and 5000.

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One Man . . . and Medicine

ARTHUR M. SACKLER, M.D.,
International Publisher, Medical Tribune

Is That Test Necessary?

THE FOUR DOCTORS at dinner one night had just finished when the youngest said, "Boy, did I get chewed out today! I didn't have a spinal tap on one of my night admissions by morning rounds."

"Are you still doing your own lab work-up at night?"

"Of course, and what a waste. It really doesn't make any sense at all. Why does every patient have to have, in addition to physical, history, urine and blood work-up, virtually automatic ECGs, x-rays, and—on the basis of a remote differential diagnosis—spinal taps?"

Status Medicine

"I've done a stint in one of the African countries which is really short in medical manpower. We were lucky to be able to do microscopics on urine, blood, and stool. There were more important things to do all the time. This is status medicine," the young doctor said. "It makes the doctor feel good and the hospital look good, but, in the over-all view, how much does it really contribute to the patient? Shouldn't my chief's question have been, Why did you do that spinal tap or the ECG or that x-ray, and not the other way around? What's 'good' in a teaching hospital could be considered 'economic exploitation' of the patient in private practice."

If you ever had a post-spinal tap headache and tinnitus and had it drag on for months, you wouldn't throw spinal taps around. I couldn't help remembering that over three decades ago it was considered good medicine at the hospital where I interned to do x-ray pelvimetry on every gravid woman. I shudder to think of the fetal and genetic damage that these routines of "scientific" or advanced medical care produced. How many things are we doing today that are comparable?

In the city of New York, hospitals were "upgraded" by attaching them to teaching institutions. This ultimately introduced the whole range of standard work-ups, soaring costs, and a situation in which hospital beds became so scarce that every day in some hospitals patients with such threatening conditions as acute hepatitis were sent back home, and misorable homes at that, to fend for themselves while others got the battery of tests.

Cost Effectiveness

Will our medical schools in the future have two types of hospitals attached—one in which the routine tests of the status institution are performed and even hooked up to computers for ultimate diagnosis and the other an institution in which doctors are trained for thoughtful clinical medicine, in which they are asked, Why did you do that procedure?—one which would make possible better and less costly medical care and a wider distribution of medical services?

The question of cost effectiveness in medicine already confronts us with increasing frequency. The other day I was shown a fabulous miracle of technology, an integrated series of diagnostic units developed for mass screening of populations. The scope of the screen was magnificent or, depending on your point of view, terrifying. The range of parameters defined constitute a list "as long as your arm." But I am afraid that I viewed the miracle with the naïve vision of a child. Good god, what would you do with all those findings? Do you have distribution curves for all these parameters? what kind of follow-up would be required for patients falling outside the so-called norms? Of course, there were no answers to these questions, for there are no easy answers to such basic problems.

Economics and Economy

Curiosity got the better of me. How much will it cost for the individual patient going through the screen?

"Oh," the answer was, "$60 to $70."

But can you sell enough of these integrated units to get into mass production, assuming that governmental agencies would want so complex a screen procedure?

"Sure, we think we can sell it to Latin-American governments interested in health."

Can you? Do you realize what percentage of the populations in some of the countries have sections of their economy with a per capita gross national product of $100 to $200 annually?

Now, Improved Machine and Reality

There was a blank look. Could it be that so simple a fact can be obscured by the beauty and glamour of our technologic intricacies?

Some time ago, in Europe, I was shown a miraculous urine analysis machine by its breathless promoter. This first "automanalyzer," I was told, could do a thousand urine analyses a day, but the next generation machine they were going to build would be able to do 10,000 urines a day. In growing astonishment I exclaimed, "Where on earth are you going to get 10,000 urine specimens a day?" And then, too, a friend to whom I told this story remarked, "And what are they going to do the day after?"

Which, of course, brings us around to the fundamental thing we have observed before—what this country needs and maybe what the world needs is not just "a good 5¢ cigar," but a lot more good, old-fashioned clinical sense and clinical medicine.

EPIGRAMS—Clinical and Otherwise

I formulate the doctrine of pathological generation...In simple terms: omnis cellula e cellua.

Rudulph Virchow (1821-1902)

Laser Use in Schools Checked for Safety

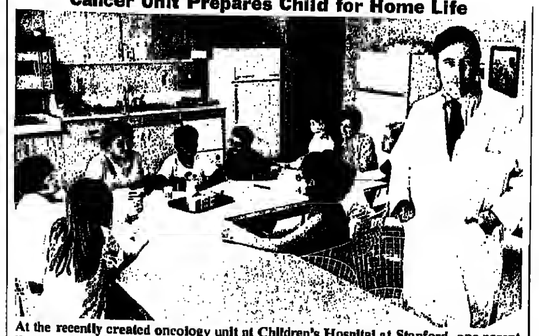
Medical Tribune Report

BETHESDA, Md.—A joint state-Federal survey in seven states has found serious shortcomings in safety practices in the use of lasers in high school and college science classes, the Food and Drug Administration announced.

Preliminary survey results have been sent to radiation control agencies in all states, the District of Columbia, Puerto Rico, and the Virgin Islands. FDA has also provided them with recommendations to improve safety in operating the light-intensifying devices and requested that the recommendations be provided to all school authorities.

The agency's Bureau of Radiological Health jointly surveyed 288 lasers with state health agencies in Colorado, Florida, Illinois, Montana, Oklahoma, Pennsylvania, and Washington. The survey was conducted in connection with the development of an FDA laser safety performance standard, now nearing completion.

Cancer Unit Prepares Child for Home Life



At the recently created oncology unit at Children's Hospital at Stanford, one parent lives with the child during hospitalization, learning to recognize changes in the child's condition and the necessary nursing duties that will be used at home after the child's release. The unit, run jointly with the pediatrics department of Stanford U. School of Medicine, is headed by Dr. Jordna Wilbur, shown with patients and parents.

2 More Doctor Units Sign Up As Unionizing Trend Grows

Continued from page 1

the county of its medical services with social service and welfare agencies.

"One of our complaints," Dr. J. Lee Aiken, president of the physicians' group, told MEDICAL TRIBUNE, "was that the county board of supervisors tried to put the county hospital under the welfare director. Furthermore, they refused to talk to the medical staff regarding patient care and hospital administration. We felt that the physicians should have some input into decisions affecting medical services.

"We decided that the formation of a union was the only way to achieve that end."

Dr. Aiken said that 54 of the less than 70 full- and half-time members of the hospital staff signed up in the Contra Costa Physicians Local 683, affiliated with the Service Employees International, A.F.L.-C.I.O.

Another Matter of Concern

Another matter of concern to the physicians, said Dr. Aiken, was the refusal of the board of supervisors to sign a contract for prepayment of Medi-Cal patients that the state government had offered the medical services.

"We feel that such a contract would result in a more efficient system that would provide better patient care at less expense to the taxpayer," he explained.

The physicians' demands, he added, are not concerned with wages or other bread-and-butter issues.

"Our primary concern," he emphasized, "is improvement of patient care and more voice in policies and decisions affecting patient care."

Alfred Dias, chairman of the county board of supervisors, said that the only demand received was one for union recognition and that this was being considered by a committee that would make its recommendations to the full board.

At the Jersey City Medical Center, 95 members of the house staff signed up to join Nursing Home and Hospital Union Local 428, affiliated with A.F.L.-C.I.O., according to the staff president, Dr. James Meehan. This, he told MEDICAL TRIBUNE, was a unanimous vote. He referred all questions regarding the physicians' demands, however, to David Solomon, attorney for both the house staff and the local.

Mr. Solomon also refused to discuss the issues but acknowledged that they included both economic matters and what he called professional privileges. He would not discuss minimum-wage demands except to say that the physicians wanted parity with physicians in New York. He also indicated that there was dissatisfaction with the present ratio of patients to physicians.

The medical center "has not and will not recognize the local," Ira C. Clark, executive director, told MEDICAL TRIBUNE, until it has followed procedures that are applicable under the state law for the authorized representation of public employees.

These, he said, would entail a petition to the New Jersey State Public Employees Relations Commission to represent the house physicians, who are public employees; a hearing that representatives of both the local and the medical center would attend; and, if the house staff wished, supervised elections.

Mr. Clark said that, since traditionally the center has recognized the house staff as a professional association and contracted with it on such issues as wages and vacations, he would want one of the options on the ballot to be the right to continue the operation of the house staff association.

In such dealings, he noted, the medical center has always been willing to allow the physicians to have outside consultants present at the meetings, but the negotiations were only between the house staff and the center and not with the outside parties.

Cold-Pressor Tests Effective Screening Of Arteriosclerosis

Continued from page 1

Then the patient's left hand was immersed in a pail of ice water for one minute and the blood pressure was measured in the right arm at 30 and 60 seconds. The highest blood pressure rise above the base-line level was considered as the maximum cold-pressor response.

Results confirmed previous findings that in the presence of arteriosclerosis alone or arteriosclerosis superimposed on hypertension, there is "significant difference" in systolic and pulse pressure cold-pressor response when compared with that of controls or of patients with hypertension alone.

Comparison of the control group with the pure hypertensive group showed no significant difference in systolic, diastolic, or pulse pressure cold-pressor response, "which suggests that the cold-pressor response of normotensive and hypertensive individuals is similar," Dr. Voudoukis observed.

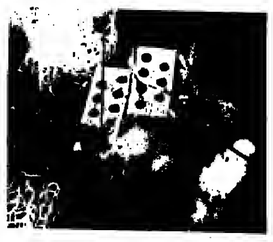
During the six-year period of the study, 20 of the 641 patients died. All had been hyperreactors to cold stimulus, and in all except one, both systolic and pulse pressure cold-pressor responses were exaggerated. All 20 had been found to have atherosclerosis or arteriosclerosis or both, and in 16 of the 20 the cause of death was either coronary heart disease or cerebrovascular disease.

"Since previous studies have demonstrated that atherosclerosis begins at an early age, it is suggested that the cold-pressor test should be done in all individuals (particularly males) of college and perhaps high school age," Dr. Voudoukis said.

Extending the boundaries of knowledge in modern brain research

Remote-control ESB:

In experiments by Delgado and associates, electrodes are implanted into specific brain areas preparatory to behavior programming by remote-control electrostimulation of the brain.



Radio-controlled ESB pinpoints action of Librium (chlordiazepoxide HCl) on selected brain areas of rhesus monkeys

Remote-control ESB (electrostimulation of the brain) elicited predictable behavior patterns in monkeys, patterns that persisted only as long as the specific stimulation was applied. Librium was then administered to determine its effect on the ESB-altered behavior patterns. Delgado and associates,[1,2] working with Librium, have helped to elucidate the CNS action of this psychotropic agent in monkeys.

Experimental observations[1,2] in monkeys* showed that:

- Librium (chlordiazepoxide HCl) blocked an electrically stimulated epileptogenic response of the amygdala, including the occurrence of an "after-discharge." Hostility of the monkey was controlled.
- Librium reduced the excitability of the monkey's central gray area, a brain structure apparently related to aggressive behavior and pain perception.
- Librium did not modify the appetite-inhibiting effects of caudate nucleus stimulation.
- Librium did not change the motor effect of internal capsule stimulation, which produced flexion of the monkey's arm and leg.
- Librium also decreased total activity in gibbons but favored normal activity such as grooming and play.

1. Delgado, J. M. R.; Bracchitta, H., and Snyder, D. R.: "Psychoactive Drugs and Radio-Controlled Behavior," film presented at the 124th Annual Meeting, American Psychiatric Association, Washington, D.C., May 3-6, 1971.
2. Delgado, J. M. R., *et al.*: "Radio Communication with the Brain," Scientific Exhibit presented at the 124th Annual Meeting, American Psychiatric Association, Washington, D.C., May 3-6, 1971.

*While the animal experiments described can be used to obtain a better understanding of the action of Librium (chlordiazepoxide HCl) in monkeys, no clinical conclusions can be drawn, as it is not possible to extrapolate animal data to humans.

Specific calming action in monkeys indicated in experimental studies

Librium®
(chlordiazepoxide HCl)

Clinical experience with Librium®
(chlordiazepoxide HCl)

After more than 12 years of wide clinical use, experience with Librium (chlordiazepoxide HCl) continues to reflect its favorable therapeutic index. By its antianxiety action, Librium can help encourage activity of ambulatory patients with deleterious anxiety and can enhance their participation in productive, recreational or rehabilitative activities.

On proper maintenance dosage, Librium generally helps calm the patient, usually without unduly interfering with mental acuity or ability to perform. When excessive anxiety has been reduced to appropriate levels, Librium therapy should be terminated.

Librium is used concomitantly with certain specific medications of other classes of drugs, such as cardiac glycosides, diuretics and antihypertensive agents, whenever anxiety is a clinically significant factor.

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Relief of anxiety and tension occurring alone or accompanying various disease states.

Contraindications: Patients with known hypersensitivity to the drug.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. As with all CNS-acting drugs, caution patients against hazardous occupations requiring complete mental alertness (*e.g.*, operating machinery, driving). Though physical and psychological dependence have rarely been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage; withdrawal symptoms (including convulsions), following discontinuation of the drug and similar to those seen with barbiturates, have been reported. Use of any drug in pregnancy, lactation, or in women of childbearing age requires that its potential benefits be weighed against its possible hazards.

Precautions: In the elderly and debilitated, and in children over six, limit to smallest effective dosage (initially 10 mg or less per day) to preclude ataxia or oversedation, increasing gradually as needed and tolerated. Not recommended in children under six. Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (*e.g.*, excitement, stimulation and acute rage) have been reported in psychiatric patients and hyperactive aggressive children. Employ usual precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship has not been established clinically.

Adverse Reactions: Drowsiness, ataxia and confusion may occur, especially in the elderly and debilitated. These are reversible in most instances by proper dosage adjustment, but are also occasionally observed at the lower dosage ranges. In a few instances syncope has been reported. Also encountered are isolated instances of skin eruptions, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased and decreased libido—all infrequent and generally controlled with dosage reduction; changes in EEG patterns (low-voltage fast activity) may appear during and after treatment; blood dyscrasias (including agranulocytosis), jaundice and hepatic dysfunction have been reported occasionally, making periodic blood counts and liver function tests advisable during protracted therapy.

Supplied: Librium® Capsules containing 5 mg, 10 mg or 25 mg chlordiazepoxide HCl.
Libritabs® Tablets containing 5 mg, 10 mg or 25 mg chlordiazepoxide.

for the relief of clinically significant anxiety in emotional and somatic disorders: a wide range of dosage options

Librium®
(chlordiazepoxide HCl)
5-mg, 10-mg, 25-mg capsules
up to 100 mg daily
in severe anxiety

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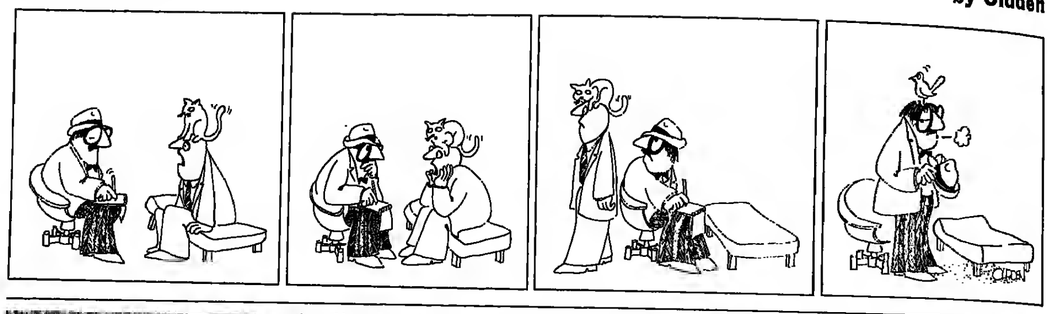
Roche Laboratories
Division of Hoffmann-La Roche Inc.
Nutley, N.J. 07110

by Oldden



SURGICAL NOTES

Surgery for Tennis Elbow

LAS VEGAS, NEV.—Tennis elbow is most often cured by rest or hormonal injections, but occasionally surgery is necessary.

Dr. Harold B. Boyd, Emeritus Professor of Orthopaedic Surgery at the University of Tennessee, said that of 871 tennis-elbow patients seen at the Campbell Clinic in Memphis over a 16-year period, only 40 did not respond to the conservative treatment and required surgery. In four patients, bilateral operations were performed.

The surgery brings relief of pain and restoration of full range of motion in almost all cases, said Dr. Boyd. The patient requires three to six months to regain full strength in the forearm. Average time for returning to work and hobbies was six weeks.

Speaking to the annual meeting of the American Academy of Orthopaedic Surgeons here, Dr. Boyd remarked that the arm is placed in a sling postoperatively, but active motion is started in 24 hours.

He remarked that probably most tennis-elbow patients are never seen by a doctor. Healing by conservative treatment usually occurs within six months, he said, and recurrences of the disorder are rare—only about 3 per cent.

Coauthor was Dr. Andin C. McLeod, Jr., of Hattiesburg, Miss.

Thromboembolic Snags

STOCKHOLM—Thromboembolic complications in major surgical interventions still constitute a serious problem, but recent studies have shown that there are possibilities of reducing their frequency, according to an editorial in a recent issue of the *Journal of the Swedish Medical Association*.

One study, it said, demonstrated that a small dose of heparin subcutaneously before and for a week after operation reduces the incidence of venothrombosis from 42 per cent to 8 per cent. Another indicated that three doses of heparin prevent postoperative thrombosis after major abdominal intervention for benign disorders just as effectively as prolonged subcutaneous heparin prophylaxis. Still another study found that dextran administered in connection with surgery reduces the thrombosis frequency by one-half in many patients.

Such preventive methods appear to be superior to therapeutic exercise or early ambulation, but before a definite stand is taken on routine prophylaxis with either heparin or dextran, it would be desirable to see the results of long-term studies on representative material, the editorial said.

High Blood Pressure

STOCKHOLM—Results with baropacing, the stimulation of the sinus nerve, in five patients with therapy-resistant severe essential hypertension were reported by Dr. Lennart Hansson, of the University of Michigan Medical Center, at the annual meeting of the Swedish Medical Society.

Electrodes were implanted bilaterally around the sinus nerve and connected to a Medtronic baropacer placed subcutaneously in the region of the pectoralis. Stimulation was aided by an external radiofrequency transmitter.

Dr. Hansson and his associates, Drs. Calvin Ernst, Stephen H. Hunyor, and Steve Julius, observed, at the onset of stimulation, a rapid drop in median arterial pressure of 22 mm. Hg. The cardiac index and heart frequency were influenced only insignificantly. Peripheral vessel resistance sank by 19 per cent.

Bill Would Let Aussie MD Record VD Patient's Name

Medical Tribune World Service

SYDNEY, AUSTRALIA—Prospective changes in Australia's Venereal Diseases Act will enable physicians, if they think it is necessary, to name a patient in official records.

Under present legislation, physicians must report every case they treat but cannot name the patient.

The Premier of New South Wales, Sir Robert Askin, said that his government, along with those of all other Australian states, has approved the preparation of a bill to bring the Act up to date.

From animal studies to clinical studies to sleep research laboratory studies in man...

Multiphasic testing documents the effectiveness and relative safety of Dalmane (flurazepam HCl) for sleep

One 30-mg capsule h.s.—usual adult dosage.
One 15-mg capsule h.s.—initial dosage for elderly or debilitated patients.

Before prescribing Dalmane (flurazepam HCl), please consult Complete Product Information, a summary of which follows:

Indications: Effective in all types of insomnia characterized by difficulty in falling asleep, frequent nocturnal awakenings and/or early morning awakening, in patients with recurring insomnia or poor sleeping habits; and in acute or chronic medical situations requiring restful sleep. Since insomnia is often transient and intermittent, prolonged administration is generally not necessary or recommended.

Contraindications: Known hypersensitivity to flurazepam HCl.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. Caution against hazardous occupations requiring complete mental alertness (e.g., operating machinery, driving). Use in women who are or may become pregnant only when potential benefits have been weighed against possible hazards. Not recommended for use in persons under 15 years of age. Though physical and psychological dependence have not been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage.

Precautions: In elderly and debilitated, initial dosage should be limited to 15 mg to preclude oversedation, dizziness and/or ataxia. If combined with other drugs having hypnotic or CNS-depressant effects, consider potential additive effects. Employ usual precautions in patients who are severely depressed, or with latent depression or suicidal tendencies. Periodic blood counts and liver and kidney function tests are advised during repeated therapy. Observe usual precautions in presence of impaired renal or hepatic function.

Adverse Reactions: Dizziness, drowsiness, lightheadedness, staggering, ataxia and falling have occurred, particularly in elderly or debilitated patients. Severe sedation, lethargy, disorientation and coma, probably dosage, have been reported. Also reported were headache, heartburn, upset stomach, nausea, vomiting, diarrhea, constipation, GI pain, nervousness, talkativeness, apprehension, irritability, weakness, palpitations, chest pains, body and joint pains and GU complaints. There have also been rare occurrences of sweating, flushes, difficulty in focusing, blurred vision, burning eyes, faintness, hypotension, shortness of breath, pruritus, skin rash, dry mouth, bitter taste, excessive salivation, anorexia, euphoria, depression, slurred speech, confusion, restlessness, hallucinations and elevated SGOT, SGPT, total and direct bilirubins and alkaline phosphatase. Paradoxical reactions, e.g., excitement, stimulation and hyperactivity, have also been reported in rare instances.

Dosage: Individualize for maximum beneficial effect. *Adults:* 30 mg usual dosage, 15 mg may suffice in some patients. *Elderly or debilitated patients:* 15 mg initially until response is determined.

Supplied: Capsules containing 15 mg or 30 mg flurazepam HCl.

ROCHE

Roche Laboratories
Division of Hoffmann-La Roche Inc
Nutley, New Jersey 07110

As confirmed in sleep research laboratory studies

- One 30-mg capsule of Dalmane (flurazepam HCl) at bedtime on average induced sleep within 17 minutes, decreased nocturnal awakenings, and provided 7 to 8 hours of sleep.
- Dalmane 30 mg was found to be effective for patients with difficulty in falling asleep, staying asleep or both.
- In studies to date, the effectiveness of Dalmane has been maintained without need to repeat or increase dosage.

As demonstrated in clinical studies

- Dalmane (flurazepam HCl) consistently reduced time required to fall asleep and increased sleep duration throughout study periods.
- Morning "hang-over" has been relatively infrequent; dizziness, drowsiness, lightheadedness and the like, were the side effects noted most frequently, particularly in elderly and debilitated patients.

Cardiomegaly May Require Digitalis Therapy

Medical Tribune Report

DALLAS, TEX.—Cardiomegaly on the chest x-ray in hypertensive heart disease signifies left ventricular failure and constitutes an indication for digitalis therapy in the asymptomatic patient, according to a study presented here by investigators from the New Jersey Medical School at the 45th annual Scientific Sessions of the American Heart Association.

Six asymptomatic patients with cardiomegaly were compared with 11 normal subjects. The patients, aged 38 to 50 years, had significant hypertension of at least four years' duration, left ventricular hypertrophy by electrocardiogram or physical examination or both, and cardiomegaly by x-ray, with cardiothoracic ratios ranging from 0.58 to 0.69. None of the patients had dyspnea on effort, edema, diastolic gallop, or rales.

While there was no significant difference between the groups in heart rate, the investigators noted that cardiac performance in terms of blood flow per beat and per minute was significantly lower in the hypertensive group.

It was noted that the patients were operating with a preload 30 per cent larger than normal; this was associated with an end-diastolic pressure of 21 mm. Hg, in contrast to 9 mm. Hg in the normals. There was also a marked reduction in the mean rate of fiber shortening during ejection in the hypertensives, "which resulted in a profound reduction in ejection fraction, and because of this subnormal emptying, end-systolic volume was approximately twice normal."

Significant Impairment Demonstrated

Measures of the contractility of the myocardium demonstrated a significant impairment in the hypertensive group, the investigators said.

When the hypertensives were subjected, by leg elevation, to a 10 per cent rise in ventricular end-diastolic volume, they reported, "the normal increase in ejection fraction and stroke volume did not occur." As a result, end-systolic volume rose significantly, "indicating inadequate emptying in response to the stress of acutely increased preload." Moreover, when they were subjected, by sustained hand grip, to a significant increase in aortic pressures, "ejection fraction and stroke volume fell." There was a further increase in residual volume, "demonstrating inadequate emptying in response to the stress of acutely increased afterload."

All these results were said to reflect impaired contractility.

Their study, the investigators declared, "demonstrates that even without the classical symptoms and signs of decompensation, contractile element failure in hypertensive heart disease can be identified by a simple noninvasive test—that is, the chest x-ray."

The authors were Drs. Ernesto Rodriguera, Ravinder Narang, E. Sultan Ahmed, James J. Fiore, and Gilbert E. Levinson.

Spina Bifida Group Forms

Medical Tribune Report

CHICAGO—The Spina Bifida Association of America was formed here recently at a meeting of 80 delegates from 27 organizations representing more than 3,000 patients with spina bifida. It will seek, among other objectives, to create a better understanding of the problems of persons with this defect. An estimated 11,000 infants are born with spina bifida each year.

MEDICAL PROGRESS

Lead Poisoning

NEWARK, N.J.—Progress in the fight to wipe out lead poisoning among children in this community has been made evident through a study of hospital admission records, according to Dr. Ann Browder, Dr. Donald B. Louria, and Morris Josetow, Ph.D., of the New Jersey Medical School.

They said that the admissions data reflected the efforts of an intensified blood-screening program started in 1969 with the development of an environmental toxicology unit of the college, working in collaboration with the Newark Department of Health and Welfare and the State Department of Health.

The analysis of hospital records showed a marked reduction in average blood-lead levels—from 130 to 86 micrograms per 100 ml.—in asymptomatic children. Intensified screening also produced about six times as many hospital admissions in 1970 (18.2 a month) as in 1967-68 (3.2 a month), mainly because many more children were being tested and treated for lead poisoning, the study found.

Sudden Death Syndrome

ADELAIDE, AUSTRALIA—Sudden death syndrome, or "cot death," has become a major contributory cause of infant mortality in South Australia, and in the age group two to seven months it now accounts for 60 per cent of all deaths, a survey here showed.

In children aged two weeks to two years, it leads the list of mortality causes, ahead of congenital malformation, infections, and accidents, said Dr. Susan Beal, a pathologist at Adelaide Children's Hospital.

Diagnosis of Hemophilia

ULM, WEST GERMANY—Early diagnosis can help increase the life expectancy of hemophiliacs, participants at the annual congress of the Hemophiliac Association of Germany were told.

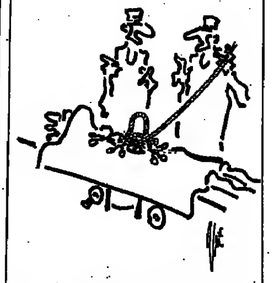
Dr. M. H. Maurer, president of the association, noted that life expectancy has increased from 15 to 40 and even 50 years with modern treatment.

The congress called for a network of treatment centers throughout West Germany to help the nation's 30,000 hemophiliacs.

Nutritional Anemia in India

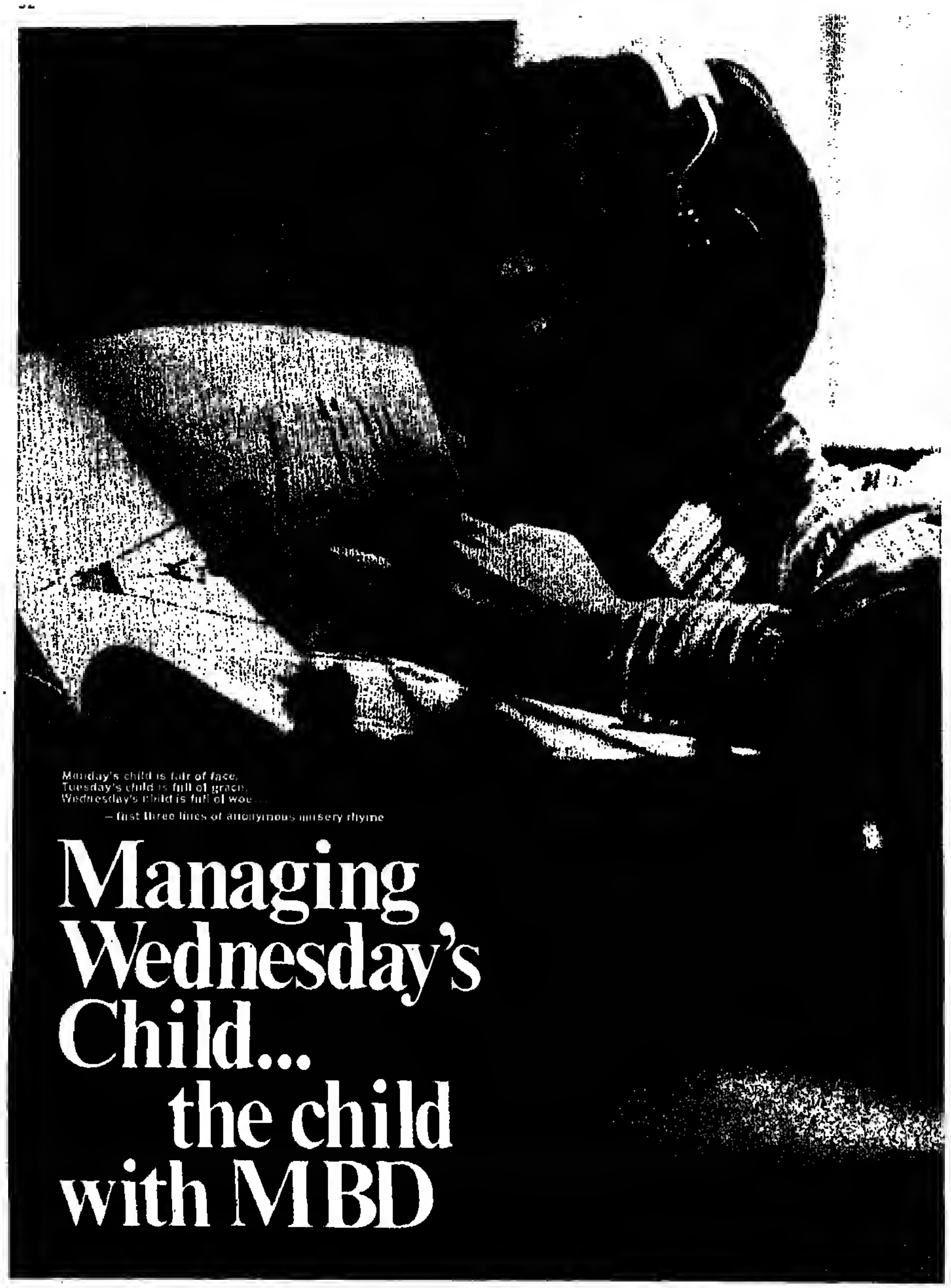
NEW DELHI—One child in two in India's population suffers from nutritional anemia, according to a survey by the Indian Council of Medical Research in association with state nutrition centers.

The survey also showed that about 50,000,000 children one to six years old are affected by protein-calorie malnutrition.



Nerves like steel cables.

© 1972 Medical Tribune



Managing Wednesday's Child... the child with MBD

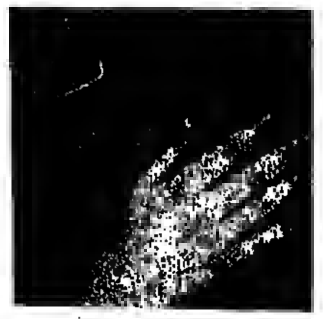
"Wednesday's child is full of woe"

It need not be this way for the MBD child.

He can learn and adjust if given a helping hand.

Without help, the MBD child may be a slow reader, can find writing difficult, and arithmetic hard to grasp. He may be excitable, and his actions can be disruptive. The result can seriously hamper his educational and social development.

But, properly diagnosed and treated, MBD—Minimal Brain Dysfunction—can be brought under control so that the afflicted child can develop normally.



And Ritalin can play an important part in the total rehabilitation program of the MBD child, which includes remedial measures at home and at school. It's currently the drug of choice in many MBD situations.[1]

Ritalin is well tolerated. It can help control the excessive motor activity of the MBD child and ameliorate behavioral and learning problems.

Of course, Ritalin is not indicated for childhood personality and behavioral disorders not associated with MBD.

Ritalin®
(methylphenidate)
only when medication is indicated

Ritalin® hydrochlorida Ⓒ
(mathylphanidate hydrochlorida)

TABLETS

INOICATION

Minimal Brain Oyslunction in Childran—as adjunctive therapy to other ramadial measuras (psychological, educational, social).

Special Oiagnostic Considerations

Specific aliology of Minimal Brain Oyslunction (MBO) is unknown, and there is no single diagnostic loal. Adequata diagnosis requiras the use not only of modical but of special psychological, educational, and social resources.

The characteristic signs most often observed are chronic history of short altention span, distractibility, emotional lability, impulsivity, and moderate to severe hyperactivity; specific learning disabilities; perceptual motor impairment; minor neurological signs and abnormal EEG. The diagnosis of MBO must be based upon a complete history and evaluation of the child and not solely on the presence of one or more of these signs.

Drug treatment is not indicated for all children with MBO. Appropriate educational placement is essential and psychological or social intervention may be necessary. When remedial measures alone are insufficient, the decision to prescribe stimulant medication will depend upon the physician's assessment of the chronicity and severity of the child's symptoms.

CONTRAINOICATIONS

Marked anxiety, tension, and agitation, since Ritalin may aggravate these symptoms. Also contraindicated in patients known to be hypersensitive to the drug and in patients with glaucoma.

WARNINGS

Ritalin is not recommended for children under six years, since safety and efficacy in this age group have not been established.

Since sufficient data on safety and efficacy of long-term use of Ritalin in children with minimal brain dysfunction are not yet available, those requiring long-term therapy should be carefully monitored.

Ritalin should not be used for severe depression of either exogenous or endogenous origin or for the prevention of normal fatigue states.

Ritalin may lower the convulsive threshold in patients with or without prior seizures; with or without prior EEG abnormalities, even in absence of seizures. Safe concomitant use of anticonvulsants and Ritalin has not been established. If seizures occur, Ritalin should be discontinued.

Use cautiously in patients with hypertension.

Drug Interactions

Ritalin may decrease the hypotensive effect of guanethidine. Use cautiously with pressor agents and MAO inhibitors. Ritalin may inhibit the metabolism of coumarin anticoagulants, anticonvulsants (phenobarbital, diphenylhydantoin, primidone), phenylbutazone, and tricyclic antidepressants (imipramine, desipramine). Downward dosage adjustments of these drugs may be required when given concomitantly with Ritalin.

Usage in Pregnancy

Adequate animal reproduction studies to establish safe use of Ritalin during pregnancy have not been conducted. Therefore, until more information is available, Ritalin should not be prescribed for women of childbearing age unless, in the opinion of the physician, the potential benefits outweigh the possible risks.

Drug Dependence

Ritalin should be given cautiously to emotionally unstable patients, such as those with a history of drug dependence or alcoholism, because such patients may increase dosage on their own initiative.

Chronically abusive use can lead to marked tolerance and psychic dependence with varying degrees of abnormal behavior. Frank psychotic episodes can occur, especially with parenteral abuse. Careful supervision is required during drug withdrawal, since severe depression as well as the effects of chronic overactivity can be unmasked. Long-term follow-up may be required because of the patient's basic personality disturbances.

PRECAUTIONS

Patients with an element of agitation may react adversely; discontinue therapy if necessary.

Periodic CBC and platelet counts are advised during prolonged therapy.

ADVERSE REACTIONS

Nervousness and insomnia are the most common adverse reactions but are usually controlled by reducing dosage and omitting the drug in the afternoon or evening. Other reactions include: hypersensitivity (including skin rash, urticaria, fever, arthralgia, exfoliative dermatitis, and erythema multiforme with histopathological findings of necrotizing vasculitis); anorexia; nausea; dizziness; palpitations; headache; dyskinesia; drowsiness; blood pressure and pulse changes, both up and down; tachycardia; angina; cardiac arrhythmias; abdominal pain; weight loss during prolonged therapy. In children, loss of appetite, abdominal pain, weight loss during prolonged therapy, insomnia, and tachycardia may occur more frequently. Toxic psychosis has been reported.

DOSAGE AND ADMINISTRATION

Children with Minimal Brain Dysfunction (6 years and over)

Start with small doses (eg, 5 mg before breakfast and lunch) with gradual increments of 5 to 10 mg weekly. Daily dosage above 60 mg is not recommended. If improvement is not observed after appropriate dosage adjustment over a one-month period, the drug should be discontinued.

If paradoxical aggravation of symptoms or other adverse effects occur, reduce dosage, or, if necessary, discontinue the drug.

Ritalin should be periodically discontinued to assess the child's condition. Improvement may be sustained when the drug is either temporarily or permanently discontinued.

Drug treatment should not and need not be indefinite and usually may be discontinued after puberty.

HOW SUPPLIED

Tablets, 20 mg (peach, scored); bottles of 100 and 1000.

Tablets, 10 mg (pale green, scored); bottles of 100, 500, 1000 and Strip Dispensers of 100.

Tablets, 5 mg (pale yellow); bottles of 100, 500, and 1000.

Consult complete product literature before prescribing.

CIBA Pharmaceutical Company
Division of CIBA-GEIGY Corporation
Summit, New Jersey 07901

Reference
1. Charlton, M. H.: Paper presented at the Annual Convention of the Medical Society of the State of New York, New York, N.Y., Feb. 7, 1971.

CIBA

Eye Exams Asked For JRA Patients By Harvard Team

Medical Tribune Report

PITTSBURGH—In view of an observed high incidence of keratoconjunctivitis sicca, occurring at various times after the onset of juvenile rheumatoid arthritis, a team of Harvard Medical School investigators "strongly urged" here that JRA patients have routine and repeated ophthalmologic examinations.

While JRA, they said, has not been previously documented as being associated with Sjögren's syndrome, they described nine patients with both disorders seen at the Robert Brigham Hospital, Boston.

"These patients were detected in a population of 250 JRA patients who have been annually evaluated with thorough examinations, including ophthalmological assessment, and were followed from four to 45 years," Drs. Jean Jackson, Larry G. Anderson, Peter H. Schur, and J. Sydney Stillman told the 18th interim scientific session of the Arthritis Foundation.

The nine patients presented with insidious-onset polyarticular disease, diagnosed at ages ranging from nine to 16 years. Keratoconjunctivitis sicca was detected from two to 48 years after the onset of the arthritis. Three patients have had iritis, and one has had corneal perforations as well.

Had Several Things in Common

All nine of the patients, the investigators reported, had the following in common: female sex, insidious onset of polyarticular arthritis and latex seropositivity.

"There were no other identifying features in their clinical presentation or laboratory parameters save for the fact that of eight patients tested for antisalivary-duct antibodies, all were positive, and this was seen in less than 15 per cent of our JRA patients who had no symptom of Sjögren's."

Salivary flow rates were decreased, it was noted, and this was corroborated by decreased salivary-glandular function as determined by scintigraphy.

Learning Medical Techniques Can Be Easy as Watching TV

Medical Tribune Report

PHILADELPHIA—Temple University School of Medicine's pilot method of educating physicians to new medical techniques provides a relaxing night of learning around the television set, according to Dr. Albert Finestone, Clinical Professor of Medicine and assistant dean for continuing education.

He uses a portable television tape recorder and a batch of instruction cassette tapes as his tools, arranges meetings with groups of general practitioners at one of their homes, and wires the recorder into the home television set.

"The first time we tried it, 10 physicians and two medical students showed up at 9:30 P.M., after office hours," he said. "It was like watching a television show, but we could stop the tape whenever we wanted to. Each tape was followed by a discussion. The physicians thought it provided an excellent opportunity at a convenient time to refresh old skills and learn new ones."

When Dr. Finestone took on the added duties of continuing education, he decided to take the programs to physicians.

"I borrowed the tape player from Roche Laboratories, the tapes from the Network for Continuing Education, and went to the doctors' homes after office hours were completed," he related.

The tapes included instruction on conducting neurologic examinations, cervical cauterization, and fiberoptics use.

"The informal atmosphere was completely effective," Dr. Finestone said. "We couldn't have done the same thing at the school during the day. "I know the physicians were excited about it. On one occasion we gathered at a physician's home where there was a color television set. The tapes are in color, and it was perfect."

Gantrisin® (sulfisoxazole) Roche® provides your patients with many important advantages:
- high urinary levels
- generally good tolerance
- high solubility at average urinary pH
- rapid absorption
- rapid renal clearance
- high plasma concentrations
- economy (average cost of therapy: less than 6½¢ per tablet)

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Nonobstructed urinary tract infections (mainly cystitis, pyelitis, pyelonephritis) due to susceptible organisms. Important Note: *In vitro* sensitivity tests not always reliable; must be coordinated with bacteriological and clinical response. Add aminobenzoic acid to follow-up culture media. Increasing frequency of resistant organisms limits usefulness of antibacterial agents, especially in chronic and recurrent urinary infections. Maximum safe total sulfonamide blood level 20 mg/100 ml; measure levels as variations may occur.

Contraindications: Hypersensitivity to sulfonamides; infants less than 2 months of age; pregnancy at term and during the nursing period.

Warnings: Safety in pregnancy not established. ... Deaths reported from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias. Sore throat, fever, pallor, purpura or jaundice may be early indications of serious blood disorders. CBC and urinalysis with careful microscopic examination should be performed frequently.

Precautions: Use cautiously in patients with impaired renal or hepatic function, severe allergy ... Hemolysis, frequently dose-related, may occur in glucose-6-phosphate dehydrogenase-deficient patients. Maintain adequate fluid intake to prevent crystalluria and stone formation.

Adverse Reactions: ...

In acute, recurrent or chronic nonobstructed cystitis

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3.

High solubility at average urinary pH
Gantrisin's unusual solubility is the main reason for its relatively low toxicity. In both free and acetylated forms, it is highly soluble at urinary pH values of 5.5 to 6.5, so there is no need for prophylactic alkali therapy.

4.

Rapid absorption
Gantrisin reaches its sites of action quickly. Measurable levels of the drug have been found in blood and urine within 30 minutes; in 2 to 3 hours, therapeutic levels usually have been reached.

5.

Rapid renal clearance
Gantrisin's rapid excretion rate is another reason why it is ... well tolerated. Over 50% of a single oral dose is excreted in 8 hours, over 90% in 24 to 48 hours, so there is ... hematuria or crystalluria, and anuria is rare. ... all sulfonamides, adequate fluid intake must be main... complete blood counts and urinalyses, with careful ... examination, should be performed frequently.

For nonobstructed cystitis due to *E. coli* and other susceptible organisms

begin with

Gantrisin®
sulfisoxazole/Roche

Usual adult dosage:
4 to 8 tablets stat
2 to 4 tablets q.i.d.

ROCHE

Diabetes Adjustment

Staff nurse Linda Taylor gives patient individualized instruction, part of the diabetes adjustment program that is currently being offered at Creighton Memorial St. Joseph Hospital in Omaha.

Biometeorologists Link Weather to Diseases

Medical Tribune World Service

LAYDEN, THE NETHERLANDS—Assertions that the weather shows a correlation with a number of diseases, ranging from asthma to mental illness, are being made by researchers in biometeorology.

The sixth International Biometeorological Congress, held at Noordwijk, the Netherlands, covered much of the latest work that has been carried out in this field. The congress attracted 220 veterinary surgeons, biologists, and meteorologists, as well as physicians, from 36 countries, including delegates from most Communist nations.

One group of doctors from a research center at the Warsaw Medical School asserted that the link between meteorologic changes and the human organism is so close that they were able to use certain hospital patients as human barometers.

Their conclusions were based on a statistical analysis of how far the various symptoms of a group of 716 patients coincided with particular types of weather conditions. The patients' disorders included 97 cases of arteriosclerosis, 102 cases of arteriosclerotic hypertension, 63 cases of myocardiopathy, and 90 cases of neurosis.

The investigators found, for instance, that blood pressure responded specifically to certain changes in meteorologic conditions. They suggested that doctors might save lives by hospitalizing patients with heart disease when meteorologists forecast hot weather accompanied by a fall in atmospheric pressure.

In a paper that attempted to explain why certain meteorologic changes cause an increased rate of sudden death from heart attacks, Dr. A. Sorban, of the Anatonic Pathology Institute of Rumania, said that studies at that institute and elsewhere have shown that a rise in temperature accompanied by a fall in atmospheric pressure reduces myocardial potassium.

Mechanism May Be Hormonal

He suggested that the mechanism of this change is a hormonal one, since there is evidence that thermal and barometric changes in the atmosphere affect the production of gonadal and cortical hormones, which play a role in the retention and elimination of potassium from the body.

"Taking into account all our data," Dr. Serban said, "we believe that the sudden variation of the myocardial potassium level, due to meteorological changes, may lead to death when myocardial and coronary lesions of a certain gravity are already present."

The effect of weather on asthmatics was among the most popular medical topics at the conference. New research carried out by scientists in the Community Health and Environmental Surveillance System of the United States Environmental Protection Agency opened up a number of questions.

Dr. Dorothy Calafiore discussed the results of a recent epidemiologic assessment of the effect of temperature and pollution on the respiratory symptoms of asthmatic and elderly patients. The survey showed that while low temperatures and high pollution levels combined to aggravate symptoms markedly, the adverse effect of air pollutants on asthmatics was greatest when minimum daily temperatures were a moderate 12.5°C. and were lowest on very cold days.

These effects, Dr. Calafiore said, were apparent in five urban and rural inland areas in the United States but were less consistent in three communities from a large Northeastern coastal district. In each community, 40 to 50 asthmatics were followed for seven or more months. Minimum temperatures alone accounted for 12 to 20 per cent of the variability in asthma attack rates inland but only 5 per cent on the coast.

It was also found that in large coastal cities, changes in temperature seemed to be closely linked with seasonal epidemics of asthma attacks, which were previously thought to be caused by air pollution.

A study of some 50 old people with obstructive lung disease also showed that both low temperatures and high air pollution aggravated their condition. Minimum temperatures accounted for up to 30 per cent of changes in the frequency of cough and phlegm.

In previous I.B.C. meetings Dr. Solcow Tromp, director of the Biometorological Research Center, Leyden, and this year's secretary of the conference, has become known for his research into the relation between asthma and atmospheric pressure.

A number of new papers added further weight to these findings—in particular, some research carried out by Prof. K. Fassol, of the Department of Pediatrics at the Tokyo Women's Medical College of Japan. The correlation between high atmospheric pressure and asthmatic attacks was demonstrated by a survey in which there was 63.4 per cent prediction in 30 cases and a 68.5 per cent prediction in 62 cases.

Blood Sedimentation Studied

Dr. Tromp's work in recent years has included study of the effects of weather and climate on blood sedimentation rate. He has found that the daily, weekly, and seasonal fluctuations in sedimentation rates correlate with the cooling index of the atmosphere. The fluctuations, he said, follow a similar pattern in albumin and globulin levels—a finding that, he suggested, could be of practical clinical significance, for related antibody substances are also probably affected to an extent that could cause periodic changes in resistance to disease.

If a person moves from a cold climate to a warm one or vice versa, he said, there will be an immediate change in the sedimentation rate and antibody level of the blood, and this perhaps explains why apparently healthy people returning from holiday often catch colds, laryngitis, or influenza.

The effect of weather on psychiatric patients was discussed by Dr. V. Faust of Basel, Switzerland. A 14-year study has shown a number of significant correlations, notably among schizophrenics, who are believed by some doctors to suffer from deficiencies in the thermoregulation mechanism because of the high number of attacks that occur in warm weather.

Similarly, it has been shown at the Leyden center that although weather probably does not have a simple and direct effect on depression and suicide, many suicide attempts do tend to take place during periods of strong atmospheric turbulence.

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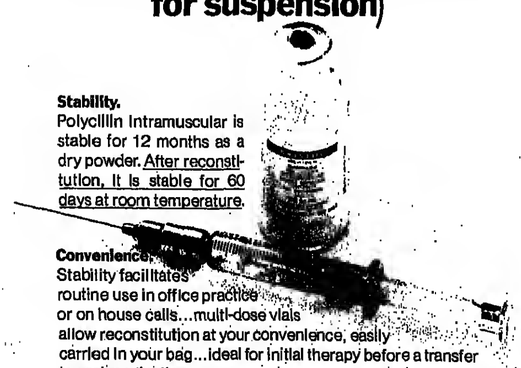

Stability.
Polycillin Intramuscular is stable for 12 months as a dry powder. After reconstitution, it is stable for 60 days at room temperature.

Convenience.
Stability facilitates routine use in office practice or on house calls...multi-dose vials allow reconstitution at your convenience, easily carried in your bag...ideal for initial therapy before a transfer to oral medication.

Economy. Stability permits use of multi-dose vials which substantially reduce the cost of delivering ampicillin by intramuscular injection; each 10-cc. vial (2.5 Gm.) contains 10 doses of 250 mg. or 5 doses of 500 mg.

BRIEF SUMMARY OF PRESCRIBING INFORMATION (1) 3/V72. For complete information consult Official Package Circular.
Indications: This drug is for intramuscular use only. Ampicillin is indicated in the treatment of susceptible strains of the following organisms in the disease listed when oral administration of ampicillin is not suitable. Culture and susceptibility studies should be performed. Indicated surgical procedures should be carried out.
Streptococci—upper respiratory infections
Pneumococci—upper and lower respiratory infections, otitis media
Staphylococci (non-penicillinase producing)—skin and soft tissue infections, respiratory tract infections
Enterococci—urinary tract and enteric infections
H. influenzae—upper and lower respiratory infections, otitis media
Proteus mirabilis—urinary tract, enteric and soft tissue infections
Neisseria gonorrhoeae—genitourinary tract infections
Shigella—enteric infections
Salmonella (including S typhosa)—enteric infections
E coli—genitourinary tract infections, skin and soft tissue infections
This intramuscular form of Polycillin is not recommended for severe infections, namely septicemia and meningitis, in which the higher serum levels attainable with Polycillin-N (sodium ampicillin) are desirable.
Contraindications: A history of allergic reactions to penicillin.
Warnings: Anaphylaxis may occur, particularly after parenteral administration and especially in patients with an allergic diathesis. Check for a history of allergy to penicillins, cephalosporins or other allergens. If an allergic or anaphylactoid reaction occurs, discontinue ampicillin and institute appropriate treatment.
Usage in Pregnancy: Safety for use in pregnancy is not established.
Precautions: Mycotic or bacterial superinfections may occur. Cases of gonorrhea with a suspected primary lesion of syphilis should have darkfield examinations before receiving treatment. In all other cases where concomitant syphilis is suspected, monthly serological tests should be performed for a minimum of 4 months. Assess renal, hepatic and hematopoietic function intermittently during long-term therapy.
Adverse Reactions: Untoward reactions include glossitis, black hairy tongue, nausea, vomiting and diarrhea, skin rashes, urticaria, exfoliative dermatitis, erythema multiforme and anaphylaxis (usually with parenteral administration). Anemia, thrombocytopenia, thrombocytopenic purpura, eosinophilia, leukopenia, and agranulocytosis have been noted, are usually reversible and are believed to be hypersensitivity phenomena. Moderate elevations in SGOT have been noted.
Usual Dosage: Respiratory Tract Infections: Adults—250 mg. q.i.d. Children—50 mg./Kg./day.
Gastrointestinal and Genitourinary Tract Infections: Adults—500 mg. q.i.d. Children—100 mg./Kg./day.
Urethritis in male adults due to *N. gonorrhoeae*: 600 mg. b.i.d.
Children weighing more than 20 Kg. should be dosed according to the adult recommendations.

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IMMATERIA MEDICA

This nettle, danger, is all over the place

Poking about in the journals has alerted us to unexpected perils that lurk in digging, playing poker, and going to the movies. A person's not safe anywhere these days.

• We've long known that archaeology and anthropology have their own peculiar occupational health hazards, but we've tended to imagine these difficulties as resulting from being incommunicado up the Whoozy River and running out of antibiotics.

Now we discover, in the *New England Journal of Medicine*, that archaeologists don't have to be up the Whoozy River after all; they can imperil their health by digging in Chico, Calif., a site not too far from either San Francisco or Sacramento, if we read our atlas correctly.

"The occupational hazard of coccidioidomycosis to archaeologists and other workers in endemic areas deserves greater recognition," says the *Journal*. It seems that of 103 students excavating some Indian ruins, "at least 61 students contracted an illness clinically compatible with coccidioidomycosis. Skin or serologic tests confirmed coccidioidomycosis in 27 of the 61." So if dig you must, watch out; and the least you can do, from our point of view, is contract a more easily spelled disease.

• Seven poker-playing patients in an English hospital ward came down with hand-foot-and-mouth disease, *Lancet* reports, observing that "the infection may have been transmitted by licking the fingers before dealing at a game of cards."

The disease was associated with Coxsackie A9 virus and was brought under control by, among other things, "halting the card games, and subsequently replacing the pack of cards."

• In Canada they have isolated a clinical entity called Dirty Harry syncope. A letter to the editor of the *Canadian Medical Association Journal* reports what we take to be a typical case history:

"I attended an elderly lady who came in with her daughter to be 'checked over' because she had fainted while watching the movie 'Dirty Harry.' . . . Fortunately she did not injure herself. . . . Before she left she told me she would never see 'Dirty Harry' again."

• • •

"In spite of our crime, pollution, political graft, and obscenity, we are still the moral leaders of the world and those countries who decry that moral leadership are often morally bankrupt themselves."

—*Cornhusker GP.*

So join our troop and start working for a merit badge for smugness.

• • •

"With each wish, however, the frantic woman entangles her husband in worse suffering until, by the last, he is inadvertently condemned to write in agony for eternity."

—*Village Voice.*

And we'll be glad to explain the horror of *that* fate to any interested persons.

• • •

We stumbled onto the following sequence of words on page 784 of the 24th edition of Dorland and pass it along as part of a campaign to combat illiteracy: **koinonia** (koi-no'ne-ah) [Gr. *koinonia* community]. 1. Associated or common action as of like cells in the same tissue. 2. Coitus.

koinonophobia (koi-no"ni-fo'be-ah) [Gr. *koinonia* community + *phobia*]. Morbid fear of a room filled with people.

koinotropic (koi'no-trop"ik) [Gr. *koinos* common + *tropos* a turning]. Syntropic, def. 3.

koinotropy. (koi-not'ro-pe). Interest in social or public relationships.

TRIBUNE SPORTS REPORT

Kentucky High Schools Have Shortage of Team Physicians

Medical Tribune Report

CINCINNATI—One-third of Kentucky high school football teams do not have team physicians, and on those that do have them, less than one-third of the players get a physical examination, a Somerset, Ky., pediatrician told the 14th National Conference on the Medical Aspects of Sports sponsored by the American Medical Association.

DR. MCLEOD

Dr. Robert N. McLeod, Jr., a high school team physician himself for 25 years and Assistant Clinical Professor of Pediatrics at the University of Kentucky College of Medicine, cited statistics obtained in a survey of coaches and players in the state's high schools by two medical students in 1970. Eighty per cent of the coaches of the 184 football teams responded to the questionnaire.

The findings included the following:

• Sixty-five per cent of the responding coaches reported that they had team physicians, yet physical examinations on these teams were performed in less than 30 per cent of the cases.

• Only 40 per cent of the teams had a physician at all home games, and a quarter of the teams had no physician scheduled for attendance at each home game.

• Of the 870 players who responded to the survey, a "significant" number (3.4 per cent) had had no preseason physical. Sixty per cent did not have a urinalysis during the physical exam.

• More than half (52.3 per cent) had been injured (mostly during practice), yet one-fourth of them did not see a physician and another 40 per cent saw a physician only after more than 24 hours had elapsed from the time of injury.

Dr. McLeod observed that it is difficult to find an adequately trained team physician in a small town, owing principally to the shortage of physicians, their lack of available time, and the insufficient financial return from such activity. Furthermore, he noted, most physicians quickly find out how inadequate their training has been, at both the graduate and postgraduate levels, to cope with the problems of sports medicine.

"I think it is imperative," he said, "to improve the status of the team physician by emphasizing the many pleasures associated with being a part of a team and its young members and by doing everything possible to improve the education of the physician. Toward this end, both medical schools in Kentucky this year will offer, for the first time, an elective in both the junior and senior years entitled 'Medical Treatment of the Athlete.'"

Dr. McLeod also called attention to the educational deficiency of many coaches in sports medicine (especially with regard to the recognition and delineation of the more serious injuries) and the frequent breakdown in communications among coach, physician, and player when a player is injured. Most high schools, Dr. McLeod noted, do not have a health coordinator, a role that trainers in larger programs handle.

new wings!

Sudden changes in mood...
disruptive behavior...
impairment of orientation

Mellaril helps calm the agitated geriatric patient. It not only reduces agitation but also diminishes anxiety, excitement, and hyperactivity. Of course, neurologic deficit cannot be repaired, but the patient with senile psychosis due to organic brain syndrome can frequently obtain meaningful symptomatic relief with Mellaril.

for the agitated geriatric with senile psychosis

Mellaril®
[thioridazine]
TABLETS: 25 mg. thioridazine HCl, U.S.P.

Before prescribing or administering, see Sandoz literature for full product information. The following is a brief summary.
Contraindications: Severe central nervous system depression, comatose states from any cause, hypotensive or hypotensive heart disease of extreme degree.
Warnings: Administer cautiously to patients who have previously exhibited a hypersensitivity reaction (e.g., blood dyscrasias, jaundice) to phenothiazines. Phenothiazines are capable of potentiating central nervous system depressants (e.g., anesthetics, opiates, alcohol, etc.) as well as atropine and phosphorus insecticides. During pregnancy, administer only when the potential benefits exceed the possible risks to mother and fetus.
Precautions: There have been infrequent reports of leukopenia and/or agranulocytosis and convulsive seizures. In epileptic patients, anticonvulsant medication should also be maintained. Pigmentary retinopathy may be avoided by remaining within the recommended limits of dosage. Administer cautiously to patients participating in activities requiring complete mental alertness (e.g., driving), and increase dosage gradually. Orthostatic hypotension is more common in females than in males. Do not use epinephrine in treating drug-induced hypotension since phenothiazines may induce a reversed epinephrine effect on occasion. Daily doses in excess of 300 mg. should be used only in severe neuropsychiatric conditions.
Adverse Reactions: *Central Nervous System*—Drowsiness, especially with large doses, early in treatment; infrequent, quantity, pseudoparkinsonism and other extrapyramidal symptoms; nocturnal confusion, hyperactivity, lethargy, psychotic reactions, restlessness, and headache. *Autonomic Nervous System*—Dryness of mouth, blurred vision, constipation, nausea, vomiting, diarrhea, nasal stuffiness, and pallor. *Endocrine System*—Galactorrhea, breast engorgement, amenorrhea, inhibition of ejaculation, and peripheral edema. *Skin*—Dermatitis and skin eruptions of the urticarial type, photosensitivity. *Cardiovascular System*—ECG changes (see *Cardiovascular Effects* below). *Other*—A single case described as parotid swelling.
The following reactions have occurred with phenothiazines and should be considered: *Autonomic Reactions*—Miosis, obstipation, anorexia, paralytic ileus. *Cutaneous Reactions*—Erythema, exfoliative dermatitis, contact dermatitis. *Blood Dyscrasias*—Agranulocytosis, leukopenia, eosinophilia, thrombocytopenia, anemia, aplastic anemia, pancytopenia. *Allergic Reactions*—Fever, laryngeal edema, angioneurotic edema, asthma. *Hepatotoxicity*—Jaundice, biliary stasis. *Cardiovascular Effects*—Changes in terminal portion of electrocardiogram, including prolongation of Q-T interval, lowering and inversion of T-wave, and appearance of a wave tentatively identified as a third T or a U wave have been observed with phenothiazines, including Mellaril (thioridazine); these appear to be reversible and due to altered repolarization, not myocardial damage. While there is no evidence of a causal relationship between these changes and significant disturbance of cardiac rhythm, several sudden and unexpected deaths apparently due to cardiac arrest have occurred in patients showing characteristic electrocardiographic changes while taking the drug. While proposed, periodic electrocardiograms are not regarded as predictive. Hypotension, rarely resulting in cardiac arrest. *Extrapyramidal Symptoms*—Akathisia, agitation, motor restlessness, dystonic reactions, trismus, torticollis, opisthotonus, oculogyric crises, tremor, muscular rigidity, and akinesia, occasionally persisting for several months or years especially in elderly patients with brain damage. *Endocrine Disturbances*—Menstrual irregularities, altered libido, gynecomastia, weight gain, false positive pregnancy tests. *Urinary Disturbances*—Retention, incontinence. *Others*—Hyperpyrexia; behavioral effects suggestive of a paradoxical reaction, including excitement, bizarre dreams, aggravation of psychoses, and toxic confusional states; following long-term treatment, a peculiar skin-eye syndrome marked by progressive pigmentation of skin or conjunctiva and/or accompanied by discoloration of exposed sclera and cornea; stellate or irregular opacities of anterior lens and cornea. 73-713
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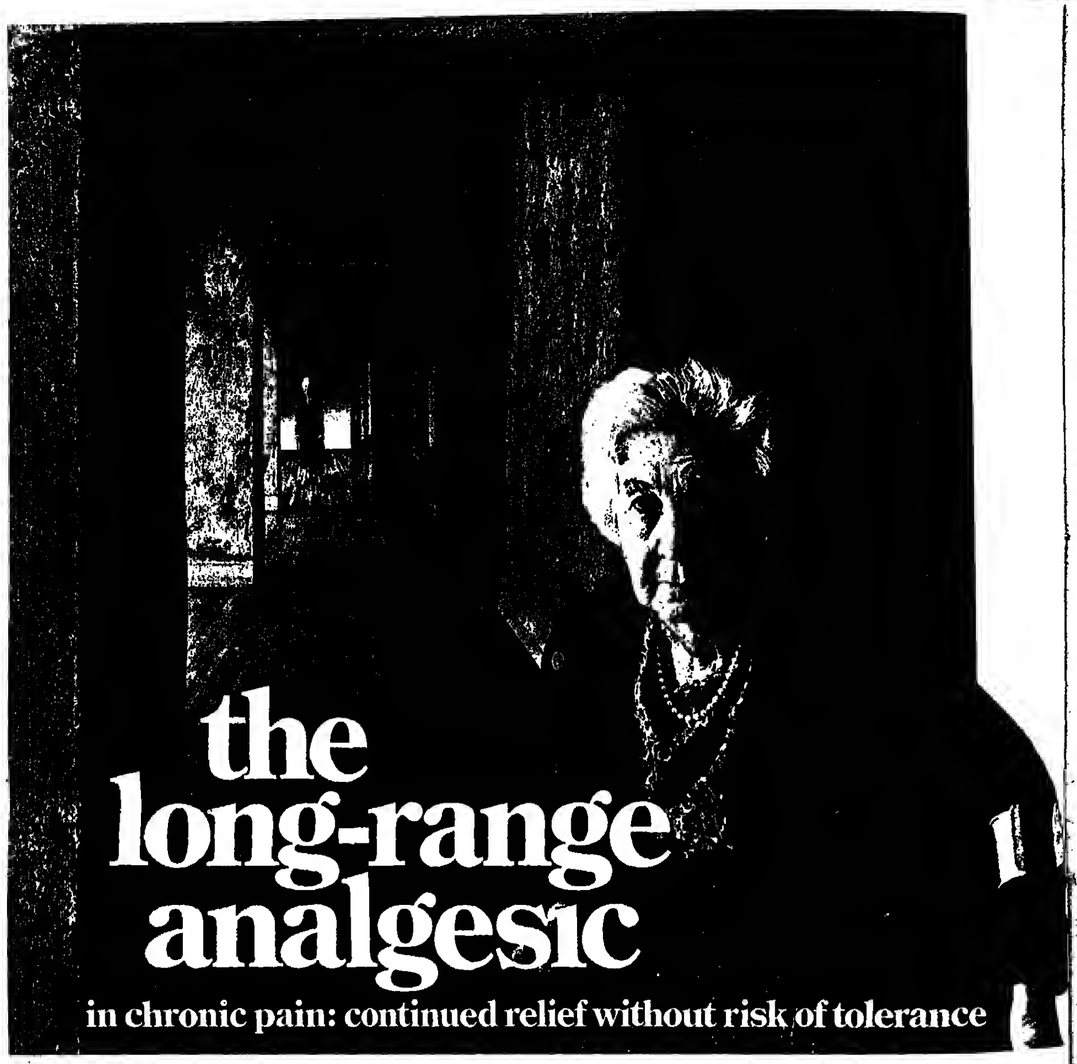

Though Talwin® Tablets can be compared to codeine in analgesic efficacy, Talwin is not subject to narcotic controls. For patients who require potent analgesia for prolonged periods, Talwin can provide consistent, long-range relief, with fewer of the consequences you've come to expect with narcotic analgesics.

- **Comparable to codeine in analgesic efficacy:** one 50 mg. Talwin Tablet appears equivalent in analgesic effect to 60 mg. (1 gr.) of codeine. Onset of significant analgesia usually occurs within 15 to 30 minutes. Analgesia is usually maintained for 3 hours or longer.
- **Tolerance not a problem:** tolerance to the analgesic effect of Talwin Tablets has not been reported, and no significant changes in clinical laboratory parameters attributable to the drug have been reported.
- **Dependence rarely a problem:** during three years of wide clinical use, only a few cases of dependence have been reported. *In prescribing Talwin for chronic use, the physician should take precautions to avoid increases in dose by the patient and to prevent the use of the drug in anticipation of pain rather than for the relief of pain.*
- **Not subject to narcotic controls:** convenient to prescribe—day or night—even by phone.
- **Generally well tolerated by most patients:** infrequently cause decrease in blood pressure or tachycardia; rarely cause respiratory depression or urinary retention; seldom cause diarrhea or constipation. If dizziness, lightheadedness, nausea or vomiting are encountered, these effects may decrease or disappear after the first few doses. (See next page of this advertisement for a complete discussion of Adverse Reactions and a Brief Summary of other Prescribing Information.)

50mg. Tablets **Talwin®**
brand of
pentazocine
(as hydrochloride)
in moderate to severe pain

in chronic pain: continued relief without risk of tolerance

Talwin® Tablets brand of pentazocine (as hydrochloride)
Analgesic for Oral Use—Brief Summary

Indications: For the relief of moderate to severe pain.

Contraindication: Talwin should not be administered to patients who are hypersensitive to it.

Warnings: *Drug Dependence. There have been instances of psychological and physical dependence on parenteral Talwin in patients with a history of drug abuse and, rarely, in patients without such a history. Abrupt discontinuance following the extended use of parenteral Talwin has resulted in withdrawal symptoms. There have been a few reports of dependence and of withdrawal symptoms with orally administered Talwin. Patients with a history of drug dependence should be under close supervision while receiving Talwin orally.*

In prescribing Talwin for chronic use, the physician should take precautions to avoid increases in dose by the patient and to prevent the use of the drug in anticipation of pain rather than for the relief of pain.

Head Injury and Increased Intracranial Pressure. The respiratory depressant effects of Talwin and its potential for elevating cerebrospinal fluid pressure may be markedly exaggerated in the presence of head injury, other intracranial lesions, or a preexisting increase in intracranial pressure. Furthermore, Talwin can produce effects which may obscure the clinical course of patients with head injuries. In such patients, Talwin must be used with extreme caution and only if its use is deemed essential.

Usage in Pregnancy. Safe use of Talwin during pregnancy (other than labor) has not been established. Animal reproduction studies have not demonstrated teratogenic or embryotoxic effects. However, Talwin should be administered to pregnant patients (other than labor) only when, in the judgment of the physician, the potential benefits outweigh the possible hazards. Patients receiving Talwin during labor have experienced no adverse effects other than those that occur with commonly used analgesics. Talwin should be used with caution in women delivering premature infants.

Acute CNS Manifestations. Patients receiving therapeutic doses of Talwin have experienced, in rare instances, hallucinations (usually visual), disorientation, and confusion which have cleared spontaneously within a period of hours. The mechanism of this reaction is not known. Such patients should be very closely observed and vital signs checked. If the drug is reinstituted it should be done with caution since the acute CNS manifestations may recur.

Usage in Children. Because clinical experience in children under 12 years of age is limited, administration of Talwin in this age group is not recommended.

Ambulatory Patients. Since sedation, dizziness, and occasional euphoria have been noted, ambulatory patients should be warned not to operate machinery, drive cars, or unnecessarily expose themselves to hazards.

Precautions: *Certain Respiratory Conditions.* Although respiratory depression has rarely been reported after oral administration of Talwin, the drug should be administered with caution to patients with respiratory depression from any cause, severe bronchial asthma and other obstructive respiratory conditions, or cyanosis.

Impaired Renal or Hepatic Function. Decreased metabolism of the drug by the liver in extensive liver disease may predispose to accentuation of side effects. Although laboratory tests have not indicated that Talwin causes or increases renal or hepatic impairment, the drug should be administered with caution to patients with such impairment.

Myocardial Infarction. As with all drugs, Talwin should be used with caution in patients with myocardial infarction who have nausea or vomiting.

Biliary Surgery. Until further experience is gained with the effects of Talwin on the sphincter of Oddi, the drug should be used with caution in patients about to undergo surgery of the biliary tract.

Patients Receiving Narcotics. Talwin is a mild narcotic antagonist. Some patients previously given narcotics, including methadone for the daily treatment of narcotic dependence, have experienced mild withdrawal symptoms after receiving Talwin.

CNS Effect. Caution should be used when Talwin is administered to patients prone to seizures; seizures have occurred in a few such patients in association with the use of Talwin although no cause and effect relationship has been established.

Adverse Reactions: Reactions reported after oral administration of Talwin include *gastrointestinal:* nausea, vomiting; infrequently constipation; and rarely abdominal distress; anorexia, diarrhea. *CNS effects:* dizziness, lightheadedness, sedation, euphoria, headache; infrequently weakness, disturbed dreams, insomnia, syncope, visual blurring and focusing difficulty, hallucinations (see *Acute CNS Manifestations* under WARNINGS); and rarely tremor, irritability, excitement, tinnitus. *Autonomic:* sweating; infrequently flushing; and rarely chills. *Allergic:* infrequently rash; and rarely urticaria, edema of the face. *Cardiovascular:* infrequently decrease in blood pressure, tachycardia. *Other:* rarely respiratory depression, urinary retention.

Dosage and Administration: *Adults.* The usual initial adult dose is 1 tablet (50 mg.) every three or four hours. This may be increased to 2 tablets (100 mg.) when needed. Total daily dosage should not exceed 600 mg.

When antiinflammatory or antipyretic effects are desired in addition to analgesia, aspirin can be administered concomitantly with Talwin.

Children Under 12 Years of Age. Since clinical experience in children under 12 years of age is limited, administration of Talwin in this age group is not recommended.

Duration of Therapy. Patients with chronic pain who have received Talwin orally for prolonged periods have not experienced withdrawal symptoms even when administration was abruptly discontinued (see WARNINGS). No tolerance to the analgesic effect has been observed. Laboratory tests of blood and urine and of liver and kidney function have revealed no significant abnormalities after prolonged administration of Talwin.

Overdosage: *Manifestations.* Clinical experience with Talwin overdosage has been insufficient to define the signs of this condition.

Treatment. Oxygen, intravenous fluids, vasopressors, and other supportive measures should be employed as indicated. Assisted or controlled ventilation should also be considered. Although nalorphine and levallorphan are *not* effective antidotes for respiratory depression due to overdosage or unusual sensitivity to Talwin, parenteral naloxone (Narcan®, available through Endo Laboratories) is a specific and effective antagonist. Talwin is not subject to narcotic controls.

How Supplied: Tablets, peach color, scored. Each tablet contains Talwin (brand of pentazocine) as hydrochloride equivalent to 50 mg. base. Bottles of 100.

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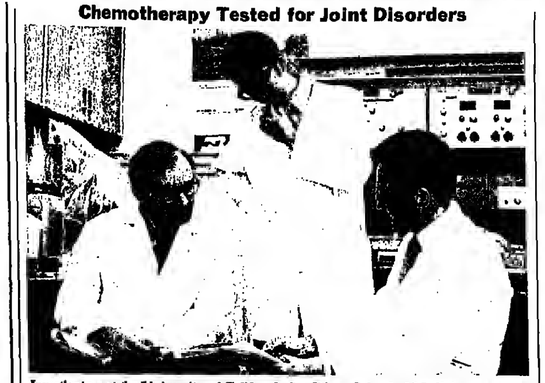
50mg. Tablets **Talwin®**
brand of
pentazocine
(as hydrochloride)
in moderate to severe pain

Chemotherapy Tested for Joint Disorders



Investigators at the University of California San Diego School of Medicine are assessing the potential of chemical treatment for preventing or reducing joint immobility. Studying data on the tissue changes that surround stiff joints are, left to right, Dr. Wayne Akeson, Professor of Surgery and head of the Division of Orthopedics, and research associates Savio Woo, Ph.D., and Dovid Amiel.

Researchers Report Progress In Altering Genetic Material

Medical Tribune Report

WASHINGTON—At concurrent sessions of the American Association for the Advancement of Science here, a biochemist from the National Institutes of Health was outlining the difficult problems that lie ahead in altering genetic material for treatment of inborn disease, while a colleague from the University of Maryland was reporting some initial success with a new technique for introducing foreign DNA into cells in tissue culture.

The NIH scientist, Dr. Robert G. Martin, said that "tissue culture alteration of human cells could come anytime now, but application to human therapy may be five or 10 years distant."

The Maryland investigator, H. Vaskon Aposhian, Ph.D., reported that he and two co-workers—S. V. S. Kashmiri and David Yelton—have been trying for three years to infect mouse and human embryonal cells in culture with a "pseudovirion." The fake virus is made by incorporating double-stranded mouse DNA into the empty capsules of polyoma viruses.

When tritiated thymidine or other suitable markers have been put into the mouse nucleic acid, Dr. Aposhian said, it has appeared in the nuclei of the infected cells, both human and mouse, but "we cannot yet demonstrate that the incorporated mouse DNA is expressed in its new host cell."

Bring Fragments of DNA

He does have evidence, he said, that when the polyoma pseudovirions are adsorbed to and enter the mammalian cells, they bring with them random fragments of DNA. Thus there is no reason in this technique why any genes should be excluded, and the chances of introducing a corrective bit of DNA are enhanced.

Dr. Martin noted that "you will have to be absolutely certain that if a viral agent is used [to transfer DNA or RNA] it is innocuous." He also noted that successful transfer of bacterial genes for galactose fermentation into human cells cultured from a patient with galactosemia has not been repeated.

"The number of genes carrying out similar functions in bacterial and human cells is probably fewer than 1,000, while the number of possible genetic diseases in man probably exceeds 100,000," Dr. Martin observed.

Other roadblocks foreseen by Dr. Martin before "genetic engineering" will be feasible include:

- Treatment for some inborn diseases would require altering a majority of the affected cells in the body. Such diseases seem to be the poorest candidates for DNA transduction.
- Treatment for a number of inborn diseases must begin in utero in order to prevent deleterious effects.
- Finally, the DNA or RNA introduced will not only have to be mammalian if it is not to be rejected by the host cells, but will probably have to be human as well.

Despite his doubts about the immediate future of "gene therapy"—not to mention his doubts about how society will regard it—Dr. Martin said: "Enormous good will come from further genetic research. Good in areas not necessarily related to inborn errors of metabolism but very possibly in afflictions like cancer and heart disease. I would continue this research at a slow but steady pace."

Frozen Marrow Cells May Retain Capacity To Yield Hemoglobin

Medical Tribune Report

BETHESDA, Md.—Human bone marrow cells stored in the frozen state as long as nine months are able to function normally in the production of hemoglobin according to investigators whose work was supported by the National Institutes of Health.

This finding, the NIH reported, brings closer the day when an individual's own previously frozen and stored marrow cells might be used to reconstitute his production of blood cells following lethal radiation or a catastrophic illness.

The capacity of such stored marrow cells to repopulate the marrow space, it noted, had been demonstrated previously in rodents, dogs, and monkeys.

Drs. John W. Adamson and Reiner Stork, of the University of Washington School of Medicine and Veterans Administration Hospital, Seattle, conducted the new studies. They tested the viability of frozen stored human bone marrow cells by determining their capacity to synthesize hemoglobin in response to treatment with erythropoietin.

In 10 laboratory studies performed on marrow from six individuals, the investigators found that hemoglobin synthesis in treated cultures was increased many times over that of untreated control cultures. Since hemoglobin synthesis takes place only in dividing and growing cells, this observation constitutes evidence that the stored cells do in fact proliferate.

The investigators cautioned that their results apply to only one of the five types of precursor or "stem" cells in the marrow.

The studies received support from the National Cancer Institute, the National Heart and Lung Institute, and the National Institute of Allergy and Infectious Diseases.

At 10:17a.m. Emmy Burns' future started looking brighter

An important step was taken to re-control her hypertension and decrease her vulnerability to organ damage

Emmy Burns just received her prescription for Ismelin. Her blood pressure was no longer responsive to milder agents. So her physician decided that this was the right time to add Ismelin. Because Ismelin is guanethidine, perhaps the most effective anti-hypertensive ever available for moderate to severe hypertension. And when blood pressure is controlled with Ismelin, it usually stays controlled.

When Ismelin is added to thiazides, increments must be gradual and dosage of all drugs reduced to lowest effective level once blood-pressure control is established.

With reduction of dosage, side effects often are minimized.

Patients should be warned about orthostatic hypotension, especially during initial dosage adjustment and with postural changes. They should avoid sudden or prolonged standing or exercise and should sit or lie down if dizzy or weak.

Uncontrolled hypertension of any degree poses an unacceptable risk to the patient's future well-being.

Ismelin® sulfate (guanethidine sulfate) sooner may be better for the uncontrolled hypertensive

BEHIND EACH CIBA PRODUCT A TRADITION OF BASIC RESEARCH

Looking for molecular "keys" to lit biological "locks," CIBA-GEIGY research chemists synthesize more than a thousand new compounds each year. By going back to the "basics"—the fundamental relationship between chemical structure and therapeutic activity—entirely new classes of drugs are developed.

CIBA

ISMELIN® sulfate
(guanethidine sulfate)
INDICATIONS: Primarily for severe or sustained elevation of blood pressure (particularly diastolic) and almost all forms of labile and progressive hypertensive disease, even when blood pressure elevation is moderate. Not recommended for labile or milder forms of hypertension.
CONTRAINDICATIONS: Proven or suspected pheochromocytoma; hypersensitivity to Ismelin. Do not use with MAO inhibitors.
WARNINGS: Ismelin is a potent drug and can lead to disturbing and serious clinical problems. Warn patients not to deviate from instructions and about the potential hazards of orthostatic hypotension, which can occur frequently. To prevent fainting, patients should sit or lie down with onset of dizziness or weakness, which may be particularly bothersome during initial dosage adjustment and with postural changes. Postural hypotension is most marked in the morning and is accentuated by hot weather, alcohol, or exercise. Warn patients to avoid sudden or prolonged standing or exercise while taking Ismelin.
Concurrent use with rauwolfia derivatives may cause excessive postural hypotension, bradycardia, and mental depression.
If possible, withdraw therapy 2 weeks prior to surgery to avoid possible vascular collapse and to reduce hazard of cardiac arrest during anesthesia. If emergency surgery is indicated, administer preanesthetic and anesthetic agents cautiously in reduced doses with oxygen, atropine, and vasopressors ready for immediate use. Give vasopressors with extreme caution because patients on Ismelin may have a greater propensity for cardiac arrhythmias.
Febrile illness may reduce dosage requirements. In frank congestive heart failure not due to hypertension, Ismelin is not recommended. Due to catecholamine depletion and increased responsiveness to norepinephrine, special care is required when treating patients with a history of bronchial asthma, since the condition may be aggravated.
Use in Pregnancy
The safety of Ismelin for use in pregnancy has not been established; therefore, this drug should be used in pregnant patients only when, in the judgment of the physician, its use is deemed essential to the welfare of the patient.
PRECAUTIONS: Give very cautiously to hypertensives with (a) renal disease with nitrogen retention; (b) coronary disease with insufficiency or recent myocardial infarction; (c) cerebral vascular disease, especially with encephalopathy; and (d) rising BUN levels. Give with extreme caution to those with severe congestive failure. Watch for weight gain or edema in patients with incipient cardiac decompensation. If digitalis is used with Ismelin, remember that both drugs slow the heart rate.
Appetite suppressants (eg, amphetamines), mild stimulants (eg, ephedrine, methylphenidate), and tricyclic antidepressants (eg, imipramine, protriptyline, doxepin) may decrease the hypotensive effect of Ismelin. Wait one week after discontinuing MAO inhibitors before starting Ismelin.
Peptic ulcers or other chronic disorders may be aggravated by a relative increase in parasympathetic tone. Periodic blood counts and liver function tests are advised during prolonged therapy.
ADVERSE REACTIONS: Frequent reactions due to sympathetic blockade—dizziness, weakness, fatigue, syncope. Frequent reactions caused by unopposed parasympathetic activity—bradycardia, increase in bowel movements, diarrhea (which may be severe and require discontinuation of the drug). Other common reactions—inhibition of ejaculation, nasal retention, edema, congestive heart failure. Less frequently—dyspnea, fatigue, nausea, vomiting, nocturia, urinary incontinence, dermatitis, scalp hair loss, dry mouth, rise in BUN, ptosis of the lids, blurring of vision, parotid tenderness, myalgia, muscle tremor, mental depression, chest pains (angina), chest anesthesias, nasal congestion, weight gain, and asthma in susceptible individuals.
DOSAGE AND ADMINISTRATION: Initial dosage should be low and increased gradually by small increments.
Before starting therapy, consult complete product literature.
HOW SUPPLIED: Tablets, 10 mg (pale yellow, scored) and 25 mg (white, scored); bottles of 100 and 1000.
CIBA Pharmaceutical Company, Division of CIBA-GEIGY Corporation, Summit, New Jersey 07901

Insomnia Study Is Facilitated By Mobile Unit

Medical Tribune World Service

BASEL, SWITZERLAND—Convinced that he could often learn much more quickly what was causing a case of insomnia by making studies in the patient's home, Dr. Ismet Karacan, director of Sleep Laboratories at the University of Florida College of Medicine, has set up a mobile unit to take the laboratory to the patient.

The equipment truck is parked within a mile radius of the patient's home. The doctor visits the patient, puts the electrodes on his head, gives him an equipment activator, and tells him to use it when he wants to go to sleep.

"The hospital laboratory can contaminate the data," Dr. Karacan told MEDICAL TRIBUNE. "You bring the subject into another social environment, an artificial environment. . . . I want to see the patient in his own environment."

Observer Spots Many Things

Even on the visit to the patient's home to set up the equipment, an observer can spot many things that may be contributing to the patient's insomnia problem, Dr. Karacan said.

"The woman sleeps in a separate bed or a separate bedroom. The family has one room, two rooms. The children are sleeping in the same room. Grandparents are living in the home. You don't get all these cues in an interview. Either they forget to tell you or they are embarrassed."

In treating insomnia, Dr. Karacan believes that drugs should be used only as a last resort. In fact, he remarked, some patients are already "walking pharmacies," administer eight or 10 drugs to themselves daily, "and if you simply take away all the drugs they are already taking, the insomnia leaves with the drugs."

"There's no question that at least 60 to 70 per cent of the self-defined insomniacs could be cured of their problem without drugs," he said. "But sometimes it takes a bit of time to find out what the real problem is. You don't often find it in a five-minute consultation, and general practitioners have very little time to talk over the problems of such patients."

For many insomniacs, Dr. Karacan continued, some changes in life style or eating and drinking habits prove to be a cure. For example, if a low arousal threshold or something else in the arousal system seems to be the cause of the insomnia, he recommends a quieter life, with avoidance of alcohol and parties and no watching of TV or reading of exciting novels before bedtime.

When such measures fail, psychoanalysis may be helpful in finding the cause of insomnia, but it is not practical for everybody, Dr. Karacan said.

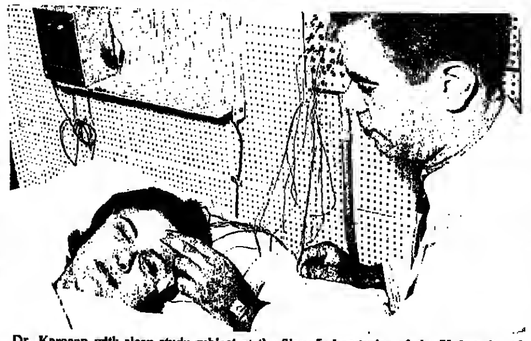
Eventually, drugs have to come into the picture for some patients. But this does not necessarily mean hypnotics. "If the problem is anxiety, you give a drug for his anxiety, not for his insomnia. And if it is depression, you give him an antidepressant, not a sleeping pill."

When, as a last resort Dr. Karacan gives a drug for the sleeping problem itself, he gives it in a pattern of five nights on the drug and two nights off it.

"So the patient doesn't sleep for two nights," he commented. "It's better than not sleeping every night and better than becoming addicted to hypnotics."

He concluded: "Insomnia is a heterogeneous group, there isn't one type of insomnia. So the treatment has to be tailor-made for each patient. A five-minute consultation and a prescription for a sleeping pill just doesn't work."

In this exclusive roundup MEDICAL TRIBUNE *is publishing highlights from the First European Congress on Sleep Research, held in Basel, Switzerland.*



Dr. Karacan with sleep study subject at the Sleep Laboratories of the University of Florida College of Medicine. Dr. Karacan also uses a mobile unit to make studies in the home environment, where the data have been found to be less contaminated.

Hypersomnia: Third Variety Said to Exist

Medical Tribune World Service

Hypersomnias have generally been classified into two types—those characterized by non-REM sleep and those in which the patient has both non-REM and REM sleep in a normal pattern but repeats the pattern over a longer period than normal.

DR. GUZMAN

A case study indicating that still another type of hypersomnia exists was presented to the Sleep Congress by Drs. R. Broughton and A. Guzman, of the University of Ottawa's Departments of Medicine and Pharmacology.

The third type, they said, is a REM hypersomnia, and it is improved by REM suppressives. Imipramine cured their patient, an 18-year-old boy, apparently permanently, they reported.

Temperature for Sleeping Is Best From 27 to 36° C.

Medical Tribune World Service

The optimal range of temperature for restful sleep is between 27° and 36° C., and the most comfortable temperature for sleeping is at the lower end of this range, according to two sleep investigators at the Neurologische Universitätsklinik mit Abteilung für Neurophysiologie, Freiburg, West Germany.

Drs. K. Kendel and W. Schmidt-Kessen said all results obtained thus far on the climatic influence on sleep had been related to extreme experimental conditions. No one had tested the influence of conditions as near normal as possible on the restful sleep of normal young adults.

Undressed Subjects Shivered

Polygraphically recording the night sleep of normal male students at varying room temperatures, they found that undressed and uncovered subjects began shivering from cold just 1° below the temperature for most comfortable rest, 27°. More than 10° higher, above 37° they began profuse sweating and reported having unpleasant heat rashes.

Among the other findings, they noted that the higher the room temperature, the more restless the sleeper, and that the heart beat went up with room temperature. On cooler nights the subjects had more REM sleep, but also, their remembrance of dreams was lower.

Cutback in REM Sleep May Curb Depression

Medical Tribune World Service

The symptoms of depression can be relieved by deprivation of REM sleep according to studies made at the Georgia Mental Health Institute, Atlanta, Ga., Dr. G. W. Vogel reported.

Sixteen patients were investigated by Dr. Vogel's research team, in an ongoing double-blind, controlled study of the hypothesis that REM sleep deprivation will relieve the symptoms of depression. The selected patients had been independently diagnosed by two psychiatrists to be suffering from moderate to severe depression without schizophrenia, drug abuse, or organic brain syndrome. Conventional sleep recordings were made nightly, and a diagnosis of endogenous or reactive depression was made by agreement of two psychiatrists.

Patients were randomly assigned to an experimental and a control group. They were deprived of REM sleep by awakenings at the start of each REM period for six consecutive nights or until they reached 30 awakenings a night, whichever came first. This was followed by a single night of uninterrupted sleep, and then the regimen of awakenings was resumed. This was done for several weeks.

Seven of Nine Improved

In the endogenous group, seven of nine subjects improved substantially during the initial three weeks of REM deprivation. With further REM deprivation, one had a relapse, while the other six improved, usually progressively, until hospital discharge six weeks from the beginning of treatment.

After discharge from the hospital—and with no antidepressant drugs—the six patients either maintained or increased their improvement. Some have now been out a year, Dr. Vogel reported, and have not relapsed.

In the reactive-depressive group, six out of seven subjects improved substantially during the initial three weeks, and with further REM deprivation five of the six continued to improve.

After discharge, and again without antidepressant drugs, three of the reactive depressives had further improvement, two had a variable course, and one required rehospitalization.

EDITORIAL CAPSULES

...brief summaries of editorials or guest editorials in current medical journals.

Daze of Retirement

Physicians should be "deeply concerned with policies that call for arbitrary retirement based on chronologic age, without regard to individual desires or capabilities."

It has been found that "retired men live an average of only two and one-half years after separation from their jobs and that the suicide rate in men past 65 is higher than in any other age group. In addition to these stark facts, the nonworker soon becomes a medical problem with most of the real or imaginary symptoms the flesh is heir to. Medicine has a vital stake in the solution to this situation, although the problem seems almost insolvable in view of the various positions taken by labor and management and in view of an increasing unemployment figure for the nation. Somewhere, somehow, for the increased health of the aging, we will have to find some way to keep them employed and motivated and wanted." Frederick C. Swartz, M.D., viewpoint. *(Geriatrics 27:30, December, 1972.)*

Progress in Leprosy

About 25 years ago, most studies on leprosy were performed by "dedicated workers, as isolated as their patients; communication was a formidable task and fraught with language difficulties. . . . However in the latter part of the 1950's and the early 1960's scientists, as distinct from humanitarian-oriented field workers, began to take an interest in the problems of leprosy. Microbiologists, statisticians, immunologists, epidemiologists and researchers in pharmaceutical companies increasingly cooperated with clinicians. . . . As a result, so much more is known about the behavior of the disease, and methods of prevention and treatment, that the control of leprosy has almost become an administrative and sociological problem rather than a purely medical one. All the problems have not been solved, but sufficient knowledge is available "about prevention, cure and rehabilitation to make the traditional public fear of the disease, and the resulting social stigma placed on the patient, no longer justifiable." Editorial. *(Med. J. Australia 2:799, October 7, 1972.)*

Misuse of Medicines

A study shows that about 75 per cent of patients at one hospital used their medicines in ways other than those prescribed. About 65 per cent took less than prescribed, and 10 per cent took more. In a considerable number of cases, this misuse of medicines was the direct result of hospitalization. Why don't patients take medicines properly? The study cited such reasons as: they forget, they can't keep track of all they are supposed to take, they feel better (or worse), they used them up, friends said they were dangerous (or worthless). What can we do about this problem? If possible, reduce polypharmacy, switch medicines to be taken only once daily, provide better information to the patient and his relatives (preferably written), and try to make the patient bring along what remains of his medicine at his next doctor's visit. Industry can help by using throwaway packaging of various types, or packaging with calendars, as for contraceptive pills. Perhaps half our patients take medicines in ways other than prescribed. It's up to each one of us to find the solution for our own patients. C. F. Borchgrevink, editorial. *(Tidsskrift for den Norske. Laegeforening* [J. Norwegian M. A.] *92:34, December 10, 1972.)*